

ISTANBUL TECHNICAL UNIVERSITY ★ GRADUATE SCHOOL

**COUPLING OZONE WITH GAC, AIX AND BIOCHAR: REMOVAL OF
PHARMACEUTICALS FROM THE BIOLOGICALLY TREATED
WASTEWATER AND FATE OF THEIR TRANSFORMATION PRODUCTS**



Ph.D. THESIS

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Department of Environmental Engineering

Environmental Science, Engineering and Management Programme

SEPTEMBER 2024

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İSTANBUL TEKNİK ÜNİVERSİTESİ ★ LİSANSÜSTÜ EĞİTİM ENSTİTÜSÜ

**OZONUN GRANÜLER AKTİF KARBON, İYON DEĞİŞİMİ VEYA
BİYOKÖMÜRLE KOMBİNASYONU İLE FARMASÖTİKLERİN BİYOLOJİK
ARITILMIŞ ATIKSUDAN GİDERİLMESİ VE TRANSFORMASYON
ÜRÜNLERİNİN AKİBETİ**

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To my son Yusuf,



FOREWORD

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ABBREVIATIONS

AIX	: Anion Exchange
AOPs	: Advanced Oxidation Processes
BAC	: Biological Activated Carbon
BV	: Bed Volume
COD	: Chemical Oxygen Demand
DOC	: Dissolved Organic Carbon
DOM	: Dissolved Organic Matter
EBCT	: Empty Bed Contact Time
EBV	: Empty Bed Volume
GAC	: Granular Activated Carbon
HRT	: Hydraulic Retention Time
IS	: Internal Standard
LOQ	: Limit of Quantification
μGAC	: Micrograin Granular Activated Carbon
MIEX	: Magnetic Ion Exchange Resin
MMBR	: Moving Bed Biofilm Reactor
NDMA	: <i>N</i> -nitrosodimethylamine
NSAIDs	: Non Steroidal Anti Inflammatory Drugs
OMPs	: Organic Micropollutants
PAC	: Powdered Activated Carbon
PFAS	: Per and Polyfluoroalkyl substances
PPCPs	: Pharmaceuticals and Personal Care Products
SBF	: Sequential Biofiltration
TOC	: Total Organic Carbon
TP	: Transformation Product
TSS	: Total Suspended Solids
UF	: Ultrafiltration
WWTP	: Wastewater Treatment Plant



SYMBOLS

Br⁻	: Bromide
BrO₃⁻	: Bromate
H₂O₂	: Hydrogen peroxide
K_{ow}	: n-octanol/water partition coefficient
M_w	: Molecular weight
NO₃-N	: Nitrate nitrogen
NH₃-N	: Ammonia nitrogen
O₃	: Ozone
•OH	: Hydroxyl radical
SUVA₂₅₄	: Specific ultraviolet absorbance at 254 nm
UV₂₅₄	: Ultraviolet absorbance at 254 nm



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COUPLING OZONE WITH GAC, AIX AND BIOCHAR: REMOVAL OF PHARMACEUTICALS FROM THE BIOLOGICALLY TREATED WASTEWATER AND FATE OF THEIR TRANSFORMATION PRODUCTS

SUMMARY

In order to prevent water pollution in the water bodies, there has been a rising interest in improving cost-efficient quaternary treatment technologies to efficiently remove pharmaceuticals from the effluents of wastewater treatment plants. Various methods, including physical, biological, and chemical processes, are being utilized to eliminate organic micropollutants (OMPs) which include pharmaceuticals and persistent pollutants such as per- and polyfluoroalkyl substances (PFAS). Among these advanced techniques, ozonation and activated carbon adsorption are currently suggested as the most feasible options for substantially decreasing pharmaceutical concentrations in the wastewaters.

Carbon-based materials such as activated carbon are notably effective adsorbents used for removing pharmaceuticals. Likewise, ozone is a highly potent oxidizing agent capable of oxidizing micropollutants directly via O_3 itself or indirectly through the generation of hydroxyl radicals. However, after ozonation, instead of being mineralized, compounds can be converted into other substances known as transformation products, which may pose greater toxicity than the original compound. Additionally, the reaction between bromide and ozone produces bromate which is a toxic and carcinogenic by-product. To mitigate potential adverse effects from ozonation, it is often recommended to implement post-treatments such as biological or adsorptive systems like granular activated carbon (GAC) to eliminate potential transformation products and by-products.

When combined with activated carbon adsorption, ozonation acts as an additional method for removing compounds that are resistant to adsorption. Crucially, activated carbon, with its extensive specific surface area and high concentration of functional groups, has demonstrated its ability to eliminate transformation products and by-products that may be generated during ozonation. While the effectiveness of the O_3 -GAC pairing is well-documented in literature, less attention has been given to combinations like ozonation with anion exchange (AIX) or other potentially more sustainable sorption materials such as biochar. The O_3 -AIX combination is particularly intriguing for this study, as many wastewater treatment plants, including the WWTP that provided wastewater for this research, are grappling with the challenge of removing PFAS.

The treated wastewater from the aforementioned WWTP is released into the Fyrisån River, which flows into Ekoln Lake, Mälaren Lake, and eventually to the Baltic Sea. Fyrisån River also contributes to replenishing a groundwater source used for the city's drinking water. Consequently, the conventionally treated wastewater, containing untreated micropollutants, is discharged into a river that ultimately serves as a drinking water source. Thus, this study aims to simulate a potential combined advanced treatment step for the wastewater treatment plant. This research is particularly

noteworthy as it not only provides guidance for implementing advanced techniques to remove micropollutants in full-scale wastewater treatment plants, but also investigates the fate of transformation products within three different combined systems: ozone and granular activated carbon filtration, ozone and ion exchange, and ozone and biochar.

The objective of this thesis was both to examine the effectiveness of removing 24 selected pharmaceuticals and to monitor the fate of 7 of their metabolites, including oxidation transformation products. This investigation utilized a combination of processes, namely O₃-GAC, O₃-biochar (with two different types of biochar), and O₃-AIX, in laboratory-scale experiments using actual effluent from a full-scale WWTP. The entire system was operated with three different O₃ dosages, each maintained continuously for two weeks. Various sorption filters, including two types of biochar (one derived from forest biomass and the other from sewage sludge), reactivated GAC, and an AIX resin, were assessed. The evaluation of results focused not only on micropollutant removal but also on the generation of transformation products and by-products. 23 out of the 24 pharmaceuticals examined were detected in the effluent wastewater collected from the Kungsängsverket WWTP in total. The findings revealed that concentrations of sertraline, trimethoprim, fluconazole, atenolol, and sulfamethoxazole were below 500 ng/L, whereas the average concentrations of venlafaxine, desvenlafaxine, fexofenadine, bicalutamide, and lamotrigine were above 5,000 ng/L.

According to the study findings, the average removal of selected pharmaceuticals varied between 8.8% and 97% with an O₃ dosage of 0.28 g O₃/g DOC, while it ranged from 86% to 99% for higher O₃ dosages (0.96 and 2.17 g O₃/g DOC). Pharmaceuticals such as fluconazole, atenolol, metoprolol, and tramadol exhibited relatively lower removal rates (9-15%) with the specific O₃ dosage of 0.28 g O₃/g DOC compared to furosemide, propranolol, clindamycin, and clarithromycin, which showed high removal rates (>90%). Tertiary amines like cetirizine and fexofenadine, known for their high reactivity with ozone, achieved removal rates of 79% and 89%, respectively, via 0.28 g O₃/g DOC in this study. Furthermore, highly reactive compounds such as carbamazepine, diclofenac, sulfamethoxazole, and trimethoprim were removed by 70%, 85%, 70%, and 88%, respectively, with 0.28 g O₃/g DOC, consistent with existing literature. Conversely, fluconazole exhibited a removal rate of 9% with an O₃ dosage of 0.28 g O₃/g DOC, while atenolol had an average removal rate of 15%.

Among all materials tested, GAC emerged as the top-performing sorbent, effectively removing nearly all compounds below the limit of quantification (LOQ) even after continuous operation for two weeks (BV=864). The potential efficacy of biochar 2 for pharmaceutical removal, which was derived from sewage sludge, was particularly significant for the overall sustainability of the WWTP. Although biochar 1 exhibited better performance than biochar 2, both sorption materials showed decreased sorption capacity over the two-week period (BV=864) for most target compounds, including carbamazepine, fexofenadine, tramadol, fluconazole, sulfamethoxazole, and erythromycin. By the end of the continuous two-week operation, biochar 1 achieved removal rates ranging between 30% and 89% (mean 68%), while biochar 2 removed selected compounds at rates of 8.5% to 82% (mean 38%). Conversely, AIX that has been included for PFAS removal, demonstrated lower removal rates as expected after two weeks compared to biochars 1 and 2, ranging between 2% and 55% (average: 20%) for positive removal rates (BV= 3,264).

Based on the findings, GAC exhibited the highest performance when paired with ozone (>99%), followed by biochar 1. Generally, the combination of ozone with biochar 1 proved to be more effective (mean=91%, range: 42-99%) than with biochar 2 (mean=79%, range: 29-99%). As anticipated, the combination of ozone with AIX yielded the lowest removal rates for pharmaceuticals (mean=58%, range: 6-98%).

Based on the findings, six out of seven metabolites were identified in samples both pre- and post-ozonation. The results suggested that while the concentrations of certain metabolites decreased during ozonation, some metabolites, including oxidation transformation products like citalopram N-oxide, exhibited an increase over the two weeks of continuous operation. On average, citalopram concentration decreased by 81%, whereas the concentration of citalopram N-oxide increased by 19% with an O₃ dosage of 0.28 g O₃/g DOC. With the system operating at 2.17 g O₃/g DOC, citalopram's average removal reached the LOQ, while the increase in citalopram N-oxide exceeded to 33%. Furthermore, all detected metabolites were eliminated to below the LOQ using GAC after two weeks of operation. Concentrations of most metabolites exhibited a linear decrease over time for biochar 1 and biochar 2, while for AIX, concentrations of certain metabolites increased over time.

During all three O₃ dosages (0.28, 0.96, and 2.17 g O₃/g DOC), bromate concentrations remained below 5 µg/L. At the lower O₃ dosage of 0.28 g O₃/g DOC, the bromide concentration in the utilized WWTP effluent was 1.03 mg/L, whereas at the higher O₃ dosages of 0.96 and 2.17 g O₃/g DOC, the bromide concentrations were 0.52 and <0.50 mg/L, respectively. This variation resulted in an inability to assess the potential formation of bromate. Removal of DOC via different O₃ dosages ranged from 19% to 26%, while GAC removed over 90% of DOC under all operational conditions. Conversely, AIX only removed less than 10% of initial DOC across all operational conditions, while in all cases, biochar 1 and biochar 2 removed within the range of 18-23% and 5-10%, respectively.

In summary, ozonation exhibited high removal efficiency of pharmaceuticals and their metabolites at higher O₃ dosages (>0.96 g O₃/g DOC), while at lower O₃ dosages (0.28 g O₃/g DOC), a post-treatment became necessary for effective pharmaceutical removal. However, higher O₃ dosages entail increased operational costs and pose a risk of transformation product formation. Therefore, employing combined systems for pharmaceutical and metabolites elimination is suggested as a preferable alternative to sole reliance on ozonation as the advanced treatment method. Comparative analysis of different post-treatment filter sorbents indicated that GAC yielded the most favorable results for pharmaceutical and metabolite removal. Conversely, the adsorption capacities of two distinct biochar types diminished over the continuous two-week operation, whereas GAC's performance remained consistent throughout. Biochar 1 outperformed biochar 2 in terms of pharmaceutical removal. AIX exhibited the lowest removal efficiencies, suggesting it may not suffice as a polishing step for ozonation when simultaneous removal of pharmaceuticals and PFAS is targeted. Overall, the combination of O₃ with GAC demonstrated the most effective performance for pharmaceutical removal. Biochar holds promise as a more sustainable substitute for GAC, as it can be sourced from renewable materials like wood. However, there is a need for ongoing development to better understand the efficacy of combined O₃-filter systems, with a focus on considering long-term operation. Before scaling up to a full-scale WWTP, conducting a life cycle assessment and feasibility analysis would be prudent steps to take.



OZONUN GRANÜLER AKTİF KARBON, İYON DEĞİŞİMİ VEYA BİYOKÖMÜRLE KOMBİNASYONU İLE FARMASÖTİKLERİN BİYOLOJİK ARITILMIŞ ATIKSUDAN GİDERİLMESİ VE TRANSFORMASYON ÜRÜNLERİNİN AKİBETİ

ÖZET

Su kirliliğini önlemek amacıyla atıksu arıtma tesislerinden ilaçları etkili bir şekilde uzaklaştırmak için, maliyet-etkin dördüncül arıtma teknolojilerini geliştirmeye olan ilgi her geçen gün artmaktadır. Bu bağlamda farmasötikler ve per- ve polifluoroalkil maddeler (PFAS) gibi kalıcı kirleticilerin de dahil olduğu organik mikrokirleticileri (OMK'lar) gidermek amacıyla çeşitli fiziksel, biyolojik ve kimyasal yöntemler geliştirilmektedir. Bu gelişmiş teknikler arasında ozonlama ve aktif karbon adsorpsiyonu, farmasötik konsantrasyonlarını önemli ölçüde azaltmak için ekonomik açıdan en uygun seçenekler olarak görülmektedir.

Aktif karbon gibi karbon bazlı malzemeler, ilaçları uzaklaştırmak için kullanılan etkili adsorbentler olarak bilinmektedir. Benzer şekilde, ozon (O_3), doğrudan veya hidroksil radikallerinin oluşturulması yoluyla organik mikrokirleticileri okside edebilen yüksek derecede etkili bir oksitleyici olarak işlev görmektedir. Ancak ozonlama neticesinde, bazı bileşikler mineralize edilmeden dönüşüm ürünleri adı verilen diğer maddelere dönüşebilmektedir. Bu durum ise orijinal bileşiğin varlığından daha yüksek bir toksisiteye neden olabilmektedir. Ayrıca, bromür ile ozon arasında gerçekleşen reaksiyon, toksik bir yan ürün olan bromatı üretmektedir. Bu bağlamda, ozonlamadan kaynaklanan potansiyel olumsuz etkileri azaltmak için genellikle biyolojik veya adsorptif sistemler gibi son işlemler uygulanması önerilmektedir. Bu sistemler, potansiyel dönüşüm ürünlerini ve yan ürünleri ortadan kaldırmaya yardımcı olmaktadır.

Aktif karbon adsorpsiyonu ile birlikte uygulandığında, ozonlama adsorpsiyona dirençli bileşikleri uzaklaştırmak için ilave bir yöntem olarak işlev görmektedir. Bunun yanı sıra, geniş özgül yüzey alanına ve yüksek konsantrasyonda fonksiyonel gruplara sahip olan aktif karbonun, ozonlama sırasında oluşabilecek dönüşüm ürünlerini ve yan ürünleri ortadan kaldırma yeteneği kanıtlanmıştır. O_3 -GAK (granüler aktif karbon) eşleşmesinin etkinliği kanıtlanmış olmasına rağmen, literatürde ozonlama ile anyon değişimi (AIX) veya ozonlama ile biyokömür gibi daha sürdürülebilir adsorpsiyon malzemeleriyle yapılan kombinasyonlarla ilgili sınırlı sayıda çalışma bulunmaktadır. Bu tez kapsamında çalışılan O_3 -AIX kombinasyonunun denenmesinin temel sebebi ise, atıksu arıtma tesislerinin birçoğunda bulunan ve giderimi oldukça zor olan PFAS gibi kirleticileri uzaklaştırmada birçok atıksu arıtma tesisine ışık tutma ihtimalinin bulunmasıdır.

Çalışmada numune temin edilen Kentsel Atıksu Arıtma Tesisinde (AAT) arıtılan atıksu, Fyrisån Nehri'ne deşarj edilmektedir. Söz konusu atıksu buradan da Ekoln Gölü'ne, Mälaren Gölü'ne ve nihayetinde Baltık Denizi'ne akmaktadır. Fyrisån Nehri ayrıca şehrin içme suyu için kullanılan yeraltı suyu kaynağını doldurmada

kullanılmaktadır. Sonuç olarak, arıtılmamış mikrokirleticileri içeren konvansiyonel olarak arıtılmış atıksu, nihayetinde içme suyu kaynağı olarak hizmet veren bir nehre deşarj edilmektedir. Bu bağlamda, bu çalışma atıksu arıtma tesisleri için potansiyel bir ileri arıtma adımının simülasyonunu amaçlamaktadır. Bu araştırmanın önemi, mikrokirleticileri tam ölçekli atıksu arıtma tesislerinden uzaklaştırmak için ileri tekniklerin uygulanmasına rehberlik etmesi ve aynı zamanda üç farklı kombine sistemde (ozon ve granüler aktif karbon filtrasyonu, ozon ve iyon değişimi ve ozon ve biyokömür) dönüşüm ürünlerinin akıbetini de araştırmasıdır.

Bu tezin amacı, seçilen 24 farmasötiğin etkin bir şekilde giderimini ve bunların oksidasyon dönüşüm ürünlerini de içeren 7 metabolitinin akıbetinin incelenmesidir. Bu çalışmada, tam ölçekli AAT'nin gerçek çıkış suyu kullanılarak laboratuvar ölçeğinde gerçekleştirilen deneylerde O₃-GAC, O₃-biyokömür (iki farklı biyokömür çeşidiyle) ve O₃-AIX kombinasyonları kullanılmıştır. Sistemde, her biri 2 hafta işletilmek üzere üç farklı O₃ dozu ile çalışılmıştır. İki farklı biyokömürden biri orman biyokütlesinden, diğeri ise atıksu çamurundan türetilmiş olup, çalışmada bu materyallerin yanısıra yeniden aktive edilmiş GAC ve bir AIX reçinesi de dahil olmak üzere çeşitli adsorpsiyon filtrelerinin performansları değerlendirilmiştir. Sonuçlar değerlendirilirken sadece mikrokirleticilerin giderimine değil, aynı zamanda dönüşüm ürünlerinin ve yan ürünlerinin oluşumuna da odaklanılmıştır.

İncelenen 24 ilacın 23'ü, Kungsängsverket AAT'den alınan çıkış atıksuyunda tespit edilmiştir. Bulgular, sertralin, trimetoprim, flukonazol, atenolol ve sülfametoksazol konsantrasyonlarının 500 ng/L'nin altında olduğunu, ancak venlafaksin, desvenlafaksin, fexofenadin, bikalutamid ve lamotriginin konsantrasyonlarının 5.000 ng/L'nin üzerinde olduğunu ortaya koymuştur.

Çalışma sonuçlarına göre, 0.28 g O₃/g ÇOK dozunda, seçilen ilaçların ortalama giderim oranları %8.8 ile %97 arasında değişirken, daha yüksek O₃ dozları için (0.96 ve 2.17 g O₃/g ÇOK) %86 ile %99 arasında değişiklik göstermiştir. Flukonazol, atenolol, metoprolol ve tramadol gibi ilaçlar, 0.28 g O₃/g ÇOK ozon dozunda, furosemid, propranolol, klindamisin ve klaritromisin gibi yüksek giderime sahip bileşiklere kıyasla daha düşük giderim verimleri göstermiştir (%9-15). Bu çalışmada, ozonla yüksek reaktiviteye sahip olan üçüncül aminlerden olan setirizin ve fexofenadin, 0.28 g O₃/g ÇOK dozunda sırasıyla %79 ve %89 giderim verimlerine ulaşmıştır. Bunun yanısıra, karbamazepin, diklofenak, sülfametoksazol ve trimetoprim gibi yüksek reaktiviteye sahip olan bileşikler, mevcut literatürle uyumlu olarak 0.28 g O₃/g ÇOK ile sırasıyla %70, %85, %70 ve %88 oranında giderilmiştir. Öte yandan flukonazol, 0.28 g O₃/g ÇOK ozon dozuyla %9'luk bir giderim oranına ulaşırken, atenolol ortalama %15 oranında giderilmiştir.

Çalışmada performansı test edilen tüm sorpsiyon malzemeleri arasında GAC en iyi performans gösteren adsorban olmuş; iki hafta sürekli işletimden sonra dahi neredeyse tüm bileşiklerin konsantrasyonunu etkili bir şekilde ölçüm limitinin (LOQ) altına düşürmüştür (YH=864). Atıksu arıtma tesisinin genel sürdürülebilirliği açısından çalışmaya dahil edilen, AAT çamurundan elde edilen biyokömür 2'nin farmasötikleri gidermede potansiyel etkinliği önem arz etmektedir. Sonuçlara göre biyokömür 1, biyokömür 2'den daha iyi performans göstermiş olup, iki haftalık örnekleme periyodu sonuçlarına göre her iki adsorpsiyon malzemesi de (YH=864) karbamazepin, fexofenadin, tramadol, flukonazol, sülfametoksazol ve eritromisin de dahil olmak üzere çoğu hedef bileşiğin giderim performansında, adsorpsiyon kapasitesinin azalmasına bağlı olarak zamanla azalma gözlemlenmiştir. İki haftalık işletim süresinin

sonunda, biyokömür 1, seçilen bileşikler %30 ile %89 arasında (%ortalama 68) giderirken, biyokömür 2, söz konusu bileşikler %8.5 ile %82 arasında (%ortalama 38) oranlarda gidermiştir. Öte yandan, PFAS uzaklaştırılması hedefiyle çalışmaya dahil edilen AIX, beklenildiği gibi, iki hafta sonunda biyokömür 1 ve 2'ye kıyasla daha düşük giderim performansı göstermiştir. AIX ile pozitif giderim verimlerini kapsayan sonuçlara göre (%BV=3,264) %2 ile %55 arasında değişen bir ortalama giderim (ortalama %20) gözlemlenmiştir.

Ozon ile 4 farklı sorpsiyon materyalinin kombinasyon sonuçları incelendiğinde, GAK'ın en yüksek performans sergilediği (ortalama %99'dan fazla) gözlemlenmiş olup, yüksek performans çerçevesinde GAK'ı biyokömür 1 takip etmiştir. Genel olarak, ozonla biyokömür 1'in kombinasyonu (ortalama=%91, aralık: %42-99) biyokömür 2 ile olan kombinasyonundan (ortalama=%79, aralık: %29-99) daha iyi performans göstermiştir. Beklenildiği gibi farmasötikler için en düşük giderim oranları ozonla AIX'in kombinasyonu neticesinde gözlemlenmiştir (ortalama=%58, aralık: %6-98).

Sonuçlara göre tüm numunelerde hem ozonlama öncesi hem de sonrasında yedi metabolitten altısı tespit edilmiştir. Bu bağlamda bazı metabolitlerin konsantrasyonlarının ozonlama sırasında azalmasına rağmen, citalopram N-oksit gibi bazı metabolitlerin konsantrasyonunun iki haftalık sürekli işletim periyodunda zamana bağlı olarak arttığı gözlemlenmiştir. 0.28 g O₃/g ÇOK'luk bir O₃ dozuyla sitalopram konsantrasyonu ortalama %81 azalırken, sitalopram N-oksit bileşiği (sitalopramla ilişkili E bileşiği)'nin konsantrasyonunun %19 arttığı tespit edilmiştir. Sistem, 2.17 g O₃/g DOC'lık bir O₃ dozunda çalıştığında ise sitalopram'ın konsantrasyonu ölçüm limitinin altına düşürülürken, sitalopram N-oksit konsantrasyonundaki artış %33'e ulaşmıştır. Çalışmada tespit edilmiş olan tüm metabolitlerin konsantrasyonu, iki hafta sürekli işletim sonunda ölçüm limitinin altına indirilmiştir. Biyokömür 1 ve biyokömür 2 için zamanla çoğu metabolitin konsantrasyonları lineer olarak azalırken, AIX için belirli metabolitlerin konsantrasyonları zamanla artmıştır.

Üç ozon dozunda da (0.28, 0.96 ve 2.17 g O₃/g ÇOK) bromat konsantrasyonları 5 µg/L'nin altında kalmıştır. Kullanılan AAT çıkış suyundaki bromür konsantrasyonu, en düşük ozon dozu olan 0.28 g O₃/g ÇOK'ta 1.03 mg/L iken, daha yüksek ozon dozları olan 0.96 ve 2.17 g O₃/g ÇOK'luk O₃ dozlarında sırasıyla 0.52 ve <0.50 mg/L olarak ölçülmüştür. Gerçek atıksudaki bu bromür konsantrasyonunun dalgalanması, bromat oluşumunun potansiyelini değerlendirmede yetersizliğe sebep olmuştur. Farklı ozon dozlarıyla ÇOK'un giderimi %19 ila %26 arasında değişirken, GAC, tüm işletim koşullarında ÇOK'un %90'ından fazlasını gidermiştir. Öte yandan AIX, tüm işletim koşullarında başlangıçtaki ÇOK'u %10'dan düşük giderirken, biyokömür 1 ve biyokömür 2 ÇOK'u tüm durumlarda sırasıyla %18-23 ve %5-10 oranlarında gidermiştir.

Özetlemek gerekirse ozonlama, yüksek O₃ dozlarında (>0.96 g O₃/g ÇOK) farmasötikleri ve metabolitlerini yüksek oranda giderirken, nispeten düşük O₃ dozunda (0.28 g O₃/g ÇOK), etkili bir farmasötik giderimi için bir son işlemin gerekli olduğu sonucuna varılmıştır. Ancak yüksek O₃ dozları ile çalışmak, artan işletme maliyetleri ve dönüşüm ürünü oluşumu riski taşımaktadır. Bu nedenle, farmasötikler ve metabolitlerinin giderimi için tek başına ozonlama yönteminin kullanılması yerine, kombinasyonlu sistemlerin kullanılması önerilmektedir. Bu çalışmada incelenmiş olan farklı son işlem filtre adsorbanlarının karşılaştırma sonuçlarına göre, farmasötiklerin ve metabolitlerinin giderilmesi için en etkili yöntemin GAK olduğu sonucuna

varılmıştır. Sonuçlara göre iki farklı biyokömür tipinin adsorpsiyon kapasiteleri, sürekli iki haftalık işletme boyunca azalmış, ancak GAK'ın performansı tüm süre boyunca kararlı kalmıştır. Biyokömür 1'in performansı, farmasötik giderimi açısından biyokömür 2'yi geride bırakırken, AIX, en düşük giderim verimlerini sergilemiştir ve ozonlama sırasında hem ilaçların hem de PFAS'ların eş zamanlı uzaklaştırılması hedeflendiğinde bir son arıtma olarak yeterli olamayacağı sonucuna varılmıştır. Genel olarak, O₃ ile GAK'ın kombinasyonu, farmasötiklerin giderimi için en etkili performansı göstermiştir.

Biyokömür, ağaç gibi yenilenebilir malzemelerden elde edilebildiğinden, GAK'a karşı daha sürdürülebilir bir alternatif olarak umut vadetmektedir. Ancak, birleşik O₃-biyokömür sistemlerinin etkinliğini daha iyi anlamak için, daha uzun süreli işletmeyi de içeren yeni araştırmaların yapılmasına ihtiyaç duyulmaktadır. Bu sistemlerin tam ölçekli bir AATT'ye uygulanmadan önce, daha kapsamlı bir laboratuvar ölçekli çalışma sonrasında pilot ölçekli sistemde incelenmesi gerekmektedir. Bunun yanı sıra, ozon ve biyokömür kombine sistemi için bir yaşam döngüsü değerlendirmesi ve fizibilite analizi yapılması önerilmektedir.

1. INTRODUCTION

Over the past thirty years, pharmaceuticals have been identified in nearly every ecological environment across all continents (Vinayagam et al., 2022). Multiple investigations worldwide have shown the existence of pharmaceuticals and their metabolites in the domestic wastewater in the past decade (Kharel et al., 2021; Reungoat et al., 2011). Pharmaceuticals are a matter of particular concern because they predominantly enter municipal wastewater treatment plants (WWTPs), where a significant portion tends to pass through the treatment processes with minimal removal (Baresel et al., 2019; Karelid et al., 2017). Consequently, pharmaceuticals are commonly found at concentrations ranging from nanograms per liter to milligrams per liter in WWTP effluents (Frascaroli et al., 2021). Due to the discharge of this treated wastewater, a wide range of pharmaceuticals has been observed in water bodies at levels that negatively affect the aquatic ecosystem (Delgado et al., 2022). In order to prevent the pollution in the water bodies, there has been a growing interest in improving cost-effective quaternary treatment technologies that are capable of efficiently eliminating pharmaceuticals from the effluents of wastewater treatment plants (Wang et al., 2016).

The effectiveness of removing pharmaceuticals is influenced by the physicochemical attributes of these compounds, such as chemical structure, volatility, acidity, lipophilicity, biodegradability, sorption potential, and the WWTPs' process configuration and operational conditions including hydraulic retention time (HRT), sludge retention time (SRT), sludge characteristics, temperature, pH, redox potential, etc. (Nas et al., 2021). Since the conventional WWTP-processes cannot remove many of the most persistent micropollutants, several advanced treatment methods have been investigated during the past two decades (Fakioglu et al., 2024). In this context, various quaternary treatment techniques including physical (adsorption, membrane filtration, reverse osmosis), biological (activated sludge, biologic activated carbon, constructed wetlands, biofilm reactor, algal reactors, microbial reactors) and chemical ozonation (O_3), coagulation, Fenton process, Photo-Fenton, photocatalysis) processes have been

employed for the removal of organic micropollutants (OMPs) including pharmaceuticals and more persistent pollutants such as per- and polyfluoroalkyl substances (PFAS) (Dhangar et al., 2020). Among these advanced treatment techniques, the suggested most cost-effective methods for substantially reducing the load of pharmaceuticals are currently ozonation and adsorption using activated carbon (Bourgin et al., 2018; Slipko et al., 2022; Östman et al., 2019).

Carbonaceous materials such as activated carbon including biochar stand out as the most effective adsorbents employed for the elimination of pharmaceuticals (Xiang et al., 2020; Zhang et al., 2022). In addition, the use of O₃-treatment has been identified as one of the most resource-efficient technologies for eliminating pharmaceuticals (Antoniou et al., 2013). Ozone is an exceptionally potent oxidizing agent which can oxidize micropollutants through either a direct reaction with O₃ or indirectly through the formation of hydroxyl radicals (Altmann et al., 2014; Granzoto et al., 2021; Guillosoy et al., 2020). However, after ozonation, rather than mineralized compounds can be transformed into other compounds named transformation products, which might be more toxic than the parent compound (Hübner et al., 2015; Gulde et al., 2021). In addition, reaction between bromide and ozone forms bromate, which is a toxic by-product. In order to decrease the potential negative impacts resulting from ozonation, it is frequently suggested to employ a post-treatment for ozonation, i.e., biological systems or adsorptive systems such as granular activated carbon (GAC), which helps to remove potential transformation and by-products (Kharel et al., 2021). If the removal of PFAS is targeted, sorption materials such as ion exchange resins are besides activated carbon the most applied treatment technology (USEPA, 2020).

With the aim of overcoming the limitations of conventional treatments to eliminate a broad spectrum of mainly pharmaceuticals, hybrid systems are recently being developed and investigated (Baresel et al., 2019; Piras et al., 2020). These systems combine biological, physical, and/or chemical treatments to improve the effectiveness of removing a diverse array of OMPs including pharmaceuticals (Dhangar et al., 2020). Applied separately or in combination, two of the most promising techniques are found to be ozonation and activated carbon by many studies over the last two decades (Bourgin et al., 2018; Ekblad et al., 2021). Combining these technologies eliminates the limitations of each individual treatment, leading to a more efficient treatment process (Granzoto et al., 2021). Ozonation serves as a supplementary method

for eliminating compounds resistant to adsorption when paired with activated carbon adsorption. Additionally, it oxidizes dissolved organic matter (DOM) to diminish competition with OMPs on activated carbon, which in turn, helps restrict the decline in activated carbon adsorption capacity over time (Guillossou et al., 2020). Most importantly, because of its large specific surface area and high content of functional groups, activated carbon has shown to also eliminate transformation products and by-products that maybe formed during ozonation (Tang et al., 2021). Although the effectiveness of at least the O₃-GAC combination is well known in the literature, combinations of ozonation with anion exchange (AIX) or other potentially more sustainable sorption materials such as biochar have not been sufficiently focused. The combination of O₃-AIX is of interest for this study as many WWTPs, including the facility that supplied wastewater for this study, also face the challenge to remove PFAS.

1.1 Purpose of Thesis

The aim of this thesis was to investigate the removal efficiency for 24 selected pharmaceuticals and the fate of 7 of their metabolites, where some of them are oxidation transformation products, using the process combination of O₃-GAC, O₃-biochar (two different types of biochar), and O₃-AIX in laboratory-scale using real effluent from a full-scale WWTP. The whole system was run with three different O₃-dosages, where at each dosage, the system was operated continuously for two weeks. As sorption filters, two different types of biochar (biochar 1 based on forest biomass and biochar 2 on sewage sludge), a reactivated GAC and an AIX resin were assessed. The results was evaluated in terms of not only the removal of micropollutants, but also the formation of transformation products and by-products.

1.2 Hypothesis

The treatment system of Uppsala Wastewater Treatment Plant (WWTP) which has an activated sludge system with biological nutrient removal (BNR). The treated wastewater is then discharged to Fyrisån River which feeds Ekoln Lake, Mälaren Lake and Baltic Sea. The Fyrisån River is used for increasing the water level of a groundwater source. The city's drinking water source is mainly this abovementioned groundwater source. Therefore, the conventionally treated wastewater which includes

the unremoved micropollutants is discharged to a river that is eventually used as a drinking water source. Therefore, this study was designed to simulate the possible polishing step for the wastewater treatment plant effluent.

This study is considered to be unique since it will not only serve as a guide for the full scale wastewater treatment plant for the removal of micropollutants with advanced techniques, but also will reveal the fate of transformation products within the designated three different combined systems which are ozone and granular activated carbon filtration, ozone and ion exchange and ozone and biochar. The combination of ozone with ion exchange or biochar sorption systems for the removal of pharmaceuticals in a continuously operated system has not been deeply focused in the existing literature. The results of the laboratory scale system which is the scope of this thesis will help better understand the applicability of the ion exchange or biochar systems into a pilot or full scale system. In other words, this study investigated the antagonistic effect between the ozonation and ion exchange or biochar processes, while having the opportunity to compare the ozone-ion exchange or ozone-biochar results with ozone-GAC results within the same study.

1.3 Literature Review

Pharmaceuticals are one of the most significant pollutants among environmental contaminants that are frequently detected in water bodies (Delgado et al., 2022). Several pathways, such as medical effluent, wastewater treatment plant (WWTP) discharge and agricultural waste are responsible for the occurrence of pharmaceuticals in soil, water, sediments and air (Vinayagam et al., 2022). As a result, there is a growing concern about the potential toxicity of pharmaceuticals to wildlife and humans that can be caused by the synergistic effects of parent compounds and metabolites present in the environment (Almuntashiri et al., 2022). The removal of these compounds from water sources is quite difficult via conventional WWTPs due to their strong hydrophilicity and weak biodegradability (Slipko et al., 2022; Vinayagam et al., 2022). Advanced treatment processes such as oxidation and adsorption which have different physical and chemical removal mechanisms are considered to improve the removal efficiencies of pharmaceuticals (Loganathan et al., 2022).

Several studies have been focused on the removal of pharmaceuticals by different advanced treatment methods (Wang and Wang, 2016) such as ozone oxidation (Ekblad et al., 2021), activated carbon adsorption (Benstoem et al., 2017; Delgado et al., 2022), ion exchange (Wang et al., 2016), membrane filtration (Alfonso-Muniozguren et al., 2021; Garcia et al., 2013), biological treatment (Lin et al., 2022; Park et al., 2022), solar treatment via photoreactor (Moreira et al., 2018) and natural treatment technologies such as constructed wetlands (Salah et al., 2023). In order to have the highest efficiency for the removal of pharmaceuticals, recent studies have focused on combining treatment methods; hereby the combination of granular or powdered activated carbon with ozone has been mostly studied (Alameddine et al. 2021; Bourgin et al. 2018; Guillossou et al. 2020; Östman et al. 2019; Vatankhah et al. 2019). Other combination studies include membrane filtration with advanced oxidation processes (Ganiyu et al., 2015; Rosman et al., 2018), membrane bioreactors with ozone (Edefell et al., 2021), combination of UV with oxidants such as ozone (Yao et al., 2018) and hydrogen peroxide (Granzoto et al., 2021).

Ozonation is one of the widely recognized techniques for its deemed capacity to remove organic micropollutants (OMPs) from municipal wastewater and is being implemented at full-scale in multiple countries (Bourgin et al., 2018; Edefell et al., 2021; Hollender et al., 2009; Itzel et al., 2020; Kharel et al., 2020; Östman et al., 2019). A variety of pharmaceuticals such as triclosan, gemfibrozil, atenolol, sulfamethoxazole, diclofenac and carbamazepine, among others have been studied by several studies in terms of removal via ozonation (Alameddine et al., 2021). According to previous bench-, pilot- and full-scale studies, a wide range of specific ozone dosage from 0.09 to 22 g O₃/g dissolved organic carbon (DOC) were studied and were able to effectively remove the most commonly existing pharmaceuticals in the wastewater by 0-100% (Alameddine et al., 2021; Bourgin et al., 2018; Edefell et al., 2021; Ekblad et al., 2021; Guillossou et al., 2020). On the other hand, several studies have combined ozonation with UV (Yao et al., 2018), catalysts (Issaka et al., 2022), electrocoagulation (Ensano et al., 2019), membrane bioreactor (Edefell et al., 2021), hydrogen peroxide as peroxone process (Yao et al., 2016) and activated carbon adsorption (Alameddine et al., 2021; Östman et al., 2019) to improve the removal of pharmaceuticals from municipal wastewaters containing recalcitrant compounds.

The most frequently utilized adsorbent for advanced wastewater treatment employed to eliminate OMPs, primarily targeting pharmaceuticals resistant to biological treatment is activated carbon, which enables the safe reuse or discharge into aquatic ecosystems. (Guillossou et al., 2020). Several types of activated carbon such as powdered activated carbon (PAC), granular activated carbon (GAC) and micro-grain activated carbon (μ GAC) have been used for the removal of pharmaceuticals (Guillossou et al., 2019). While GAC has been usually applied solely for the adsorptive removal of OMPs from wastewater (Altmann et al., 2016), PAC was applied in combination with ultrafiltration (UF) for the removal of several OMPs including pharmaceuticals (Margot et al., 2013). Other sorption methods such as biochar have also been investigated by several researchers for the removal of OMPs including pharmaceuticals (Shin et al., 2020; Hagemann et al., 2020; Li et al., 2022; Xiang et al., 2020). For instance, Hagemann et al. (2020) investigated the performance of biochar in the removal of pharmaceuticals, where biochar was applied to biologically treated wastewater as an alternative to activated carbon from fossil precursors. Conversely, numerous research studies have highlighted the significant capability of commercial anion exchange resins (AIXs) in effectively eliminating pharmaceutical compounds from different water sources (Michael-Kordatou et al., 2015). The combination of these sorption methods with other treatment techniques might increase the effectiveness of the removal of pharmaceuticals.

Adsorption and ozonation are two advanced treatment processes with particular removal mechanisms utilized to remove OMPs, where their effectiveness relies on the strength and kinetics of ozonation (ozone molecule and OH radical ($\text{OH}\cdot$) reaction) along with the adsorption kinetics of the individual OMPs (Loganathan et al., 2022). The combination of ozonation and activated carbon is a widely recognized practice that is already implemented at full-scale in certain WWTPs, where ozonation plays the primary role in removing OMPs, accompanied with adsorption, primarily using granular activated carbon (GAC) as an additional post-treatment step. When coupled with activated carbon adsorption, ozonation serves as a complementary process for the removal of compounds that are resistant to adsorption, as well as oxidizing dissolved organic matter (DOM) to reduce the competition with OMPs and their transformation products onto activated carbon which enables to limit the activated carbon adsorption capacity decrease over time (Guillossou et al., 2020). When these two technologies are

combined, the limitations of each single treatment are reduced and the treatment train becomes more efficient (Granzoto et al., 2021). Additionally, adsorption via GAC can not only remove unoxidized pollutants but also the byproducts of ozonation, some of which are suspected to be human carcinogens (Loganathan et al., 2022).

1.3.1 Classification of pharmaceuticals in wastewater

The most frequently detected pharmaceuticals in the municipal wastewaters can be classified as antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), anticonvulsants, antifungals, lipid regulators, cardiovascular agents, beta-blockers, antidepressants, synthetic hormones, contrast media agents and analgesics (Wang and Wang, 2016). The pharmaceutical classes along with their function, common representatives and physicochemical properties are presented in Table 1.1.

Table 1.1 : Classification of commonly studied pharmaceuticals in wastewater. Adapted from Wang and Wang (2016)^a.

Pharmaceuticals	Function	Common representatives	Molecular weight	Log K_{ow}^b
Antibiotics	Bacteria inactivation	Sulfamethoxazole	253.3	0.89
		Trimethoprim	290.3	0.91
		Amoxicilin	365.4	0.87
		Erythromycin	733.9	3.06
		Ofloxacin	361.4	-0.39
		Ciprofloxacin	331.3	0.28
		Ampicillin	349.4	1.45
		Doxycycline	444.4	-0.02
		Tylosin	916.1	1.63
		Enoxacin	320.1	-0.2
		Sulfapyridine	250.3	0.35
		Cefalexin	347.4	0.65
		Cefaclor	367.8	0.4
		Mecilinam	325.4	1.3
		Tetracycline	444.4	-1.37
		Clarithromycin	747.9	3.16
		Chloramphenicol	323.1	1.14
		Clindamycin	424.9	NA
NSAIDs	Inflammation reduction and pain relief	Ibuprofen	206.3	3.97
		Diclofenac	296.1	4.51
		Acetaminophen	151.2	0.46
		Aspirin	180.2	1.19
		Indomethacin	357.8	4.27
		Naproxen	230.3	3.18
		Nimesulide	308.3	2.6
		Phenazone	188.2	0.38
		Salicylic acid	138.1	2.26
		Paracetamol	151.2	0.33
		Ketoprofen	254.3	2.8

Table 1.1 (continued): Classification of commonly studied pharmaceuticals in wastewater. Adapted from Wang and Wang (2016)^a.

Pharmaceuticals	Function	Common representatives	Molecular weight	Log K_{ow} ^b
Anticonvulsants	Psychiatric support	Carbamazepine	236.3	2.25
		Primidone	218.3	1.12
		Dilantin	252.3	2.47
		Phenobarbital	232.2	1.47
		Cabapentin	171.2	-1.1
		Phenytoin	252.3	2.47
Antifungals	Treatment of fungal infections	Fluconazole	306.3	0.25
		Triclosan	289.5	4.76
Lipid regulators	Regulation of triglycerides and cholesterol in blood	Clofibrate	242.7	3.02
		Benzafibrate	361.8	3.61
		Clorfibric acid	214.6	2.88
		Gemfibrozil	250.3	4.77
		Simvastatin	418.6	4.68
		Furosemide	330.7	1.51
Cardiovascular agents	Treatment of heart or the circulatory system	Irbesartan	428.5	1.13
		Losartan	422.9	4.01
		Metoprolol	267.4	1.88
Beta-blockers	Inhibition of adrenalin and noradrenalin	Atenolol	266.3	0.16
		Metoprolol	267.4	9.7
		Nadolol	309.4	-0.6
		Pindolol	248.3	1.75
		Acebutolol	336.4	1.71
		Propanolol	259.3	3.48
		Sotalol	272.4	0.24
Antidepressants	Treatment of depression	Diazepam	284.7	3.08
		Doxepin	279.4	3.84
		Imipramine	280.4	4.28
		Amitriptyline	277.4	4.81
		Fluxetine	309.3	3.96
		Meprobamate	218.3	0.93
		Oxazepam	286.7	2.92
		Thioridazine	370.6	5.90
		Sertraline	306.2	5.29
		Venlafaxine	277.4	3.20
Synthetic hormones	Regulation of metabolism and development	Estriol	288.4	2.45
		Mestranol	310.4	4.68
		Estrone	270.4	3.13
		17- β Estradiol	272.4	4.01
		Testosterone	288.2	3.32
Contrast media agents	Enhancement of vascular for MR	Iopromide	791.1	-2.1
		Iomeprol	777.1	NA
		Diatrizoate acid	613.9	1.37
Analgesics	Pain relief	Tramadol	263.4	3.01

^a NA = not available. ^b K_{ow} = n-octanol/water partition coefficient.

The removal mechanism of the pharmaceuticals can be chemical (oxidation), physical (adsorption) or biological (biological degradation). For instance, the ozone oxidation mechanism is highly dependent on the chemical bonds of the target pharmaceuticals. Ozone tends to react with the electron donating (withdrawing) molecular groups such as —OH, —NH₂, while the possibility to react with the electron acceptors (—COOH, —NO₂, —Cl) such as itself is really low (von Sonntag and von Gunten, 2012). On the

other hand, the polarity of the compound plays an important role in the activated carbon adsorption process, where n-octanol/water partition coefficient ($\log K_{ow}$) of the compound might indicate whether the compound tends to be adsorbed from the water phase to the solid phase (Table 1.1). A compound having $\log K_{ow}$ lower than one means it is more soluble in water (Amézqueta et al., 2020). For instance, carbamazepine and diclofenac have shown very high adsorbability due to their high $\log K_{ow}$ values at 2.25 and 4.51, while sulfamethoxazole shows moderate or low adsorbability due to low $\log K_{ow}$ at 0.89 (Amézqueta et al., 2020). Substances with high $\log K_{ow}$ values have a better adsorbability rate than the ones with low $\log K_{ow}$ values (Golovko et al., 2020). The most commonly detected pharmaceuticals in wastewater treatment plants are listed in Table 1.2 according to their chemical class. These pharmaceuticals have a wide range of different structural properties which often contain aromatic groups including phenyl, pyrimidine and lactone rings and heterocyclic structures along with having several double bonds.

Table 1.2 : Several commonly detected pharmaceuticals in WWTPs according to their chemical class. Adapted from Frascaroli et al. (2021).

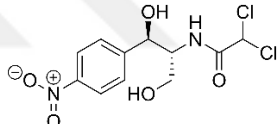
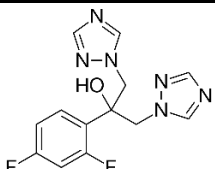
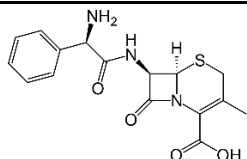
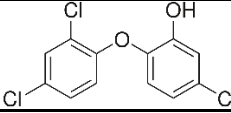
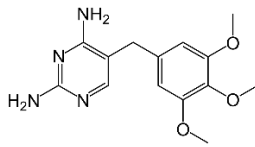
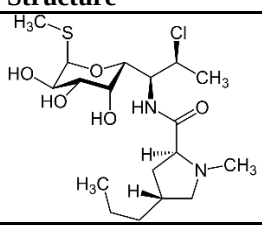
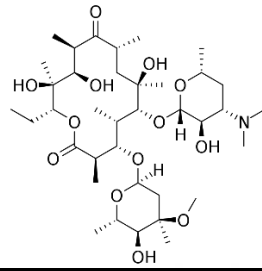
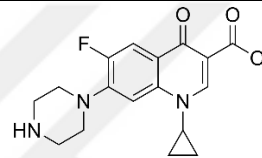
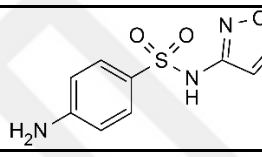
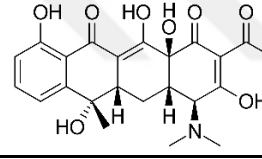
Pharmaceutical	Class	Properties	Structure
Chloramphenicol	Amphenicols	Phenylpropanoid structure	
Fluconazole	Azoles	Heterocyclic, contains double bonds and N atom	
Cefalexin	Cephalosporins	Contains 6-membered dihydrothiazine ring	
Triclosan	Diphenylethers	Contains two phenyl rings	
Trimethoprim	Diaminopyrimidines	Contains two amine groups on a pyrimidine ring	

Table 1.2 (continued): Several commonly detected pharmaceuticals in WWTPs according to their chemical class. Adapted from Frascaroli et al. (2021).

Pharmaceutical	Class	Properties	Structure
Clindamycin	Lincosamides	Contains pyrrolidine ring linked to pyranose moiety via amide bond	
Erythromycin	Macrolides	Consist of large macrocyclic lactone ring	
Ciprofloxacin	Quinolones	Contains bicyclic core structure	
Sulfamethoxazole	Sulfonamides	Contains sulfonamide group	
Tetracycline	Tetracyclines	Contains four hydrocarbon rings	

1.3.2 Ozone oxidation

1.3.2.1 Ozonation system

Ozonation is generally applied after the secondary effluent of the WWTPs (Figure 2.1) to reduce the scavenging of ozone by the organic fraction that is present in the wastewater (Hollender et al., 2009; Schaar et al., 2010). During ozonation, oxidation occurs by either direct reactions with ozone molecule or via formed hydroxyl radicals at several reaction rates (Edefell et al., 2021). Ozone itself is a selective oxidant which is highly reactive that reacts with secondary and tertiary amines, activated aromatic rings and olefins which all have electron-rich moieties (von Sonntag and von Gunten, 2012). Therefore, in biologically treated wastewater, ozone reacts with numerous OMPs (Lee et al., 2013) and inclines to react with electron-rich moieties, including aromatic rings, amines and certain double bonds (von Sonntag and von Gunten, 2012). Furthermore, the removal of OMPs depends on the structure of the substance, for

instance, carbamazepine and diclofenac have been shown to have a higher reactivity with ozone than oxazepam (Ekblad et al., 2021). On the other hand, the self-decomposition of ozone leads to the formation of hydroxyl radicals ($\cdot\text{OH}$) which is a non-selective oxidant and can react with amides, alkanes and non-activated aromatic compounds (Guillossou et al., 2020).

The structure of some commonly studied pharmaceuticals and their second-order reaction rate constant with ozone and $\cdot\text{OH}$ are given in Table 1.3. The pharmaceuticals were divided into 4 groups according to their ozone second-order rate constants, where the removal by ozonation is considered high for group I, intermediate for group II and III and low for group IV.

Table 1.3 : Structure of the selected pharmaceuticals and their second-order reaction rate constant with ozone and $\cdot\text{OH}$. Adapted from Lee et al. (2013) and Alameddine et al. (2021).

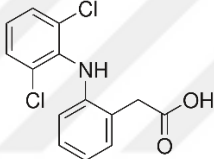
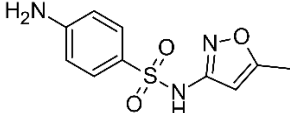
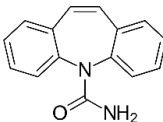
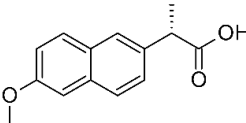
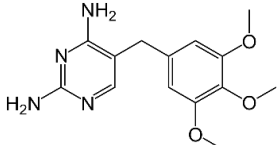
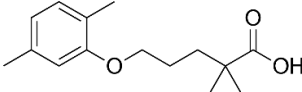
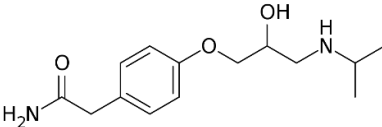
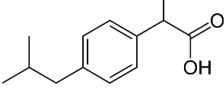
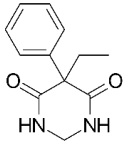
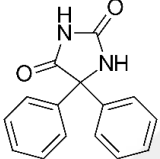
Name Formula	Structure	$k_{\text{O}_3}, \text{pH}=7^a$ $\text{M}^{-1} \text{s}^{-1}$	$k_{\text{O}_3}^b$ $\text{M}^{-1} \text{s}^{-1}$	k_{OH}^c $\text{M}^{-1} \text{s}^{-1}$
Group I : $k_{\text{O}_3}, \text{pH}=7 > 1 \times 10^5 \text{ M}^{-1} \text{s}^{-1}$				
Diclofenac $\text{C}_{14}\text{H}_{11}\text{Cl}_2\text{NO}_2$		1×10^6	1×10^6	7.5×10^9
Sulfamethoxazole $\text{C}_{10}\text{H}_{11}\text{N}_3\text{O}_3\text{S}$		5.7×10^5	5.7×10^5	5.5×10^9
Carbamazepine $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}$		3×10^5	3×10^5	8.8×10^9
Naproxen $\text{C}_{14}\text{H}_{14}\text{O}_3$		2×10^5	2×10^5	9.6×10^9
Trimethoprim $\text{C}_{14}\text{H}_{18}\text{N}_4\text{O}_3$		2.7×10^5	5.2×10^5	6.9×10^9
Group II : $1 \text{ M}^{-1} \text{s}^{-1} < k_{\text{O}_3}, \text{pH}=7 < 1 \times 10^5 \text{ M}^{-1} \text{s}^{-1}$				
Gemfibrozil $\text{C}_{15}\text{H}_{22}\text{O}_3$		$\sim 5 \times 10^4$	$\sim 5 \times 10^4$	10×10^9
Atenolol $\text{C}_{14}\text{H}_{22}\text{N}_2\text{O}_3$		1.7×10^3	6.3×10^5	8×10^9

Table 1.3 (continued): Structure of the selected pharmaceuticals and their second-order reaction rate constant with ozone and $\cdot\text{OH}$. Adapted from Lee et al. (2013) and Alameddine et al. (2021).

Name Formula	Structure	$k_{\text{O}_3, \text{pH}=7}^{\text{a}}$ $\text{M}^{-1} \text{s}^{-1}$	$k_{\text{O}_3}^{\text{b}}$ $\text{M}^{-1} \text{s}^{-1}$	k_{OH}^{c} $\text{M}^{-1} \text{s}^{-1}$
Group III : $k_{\text{O}_3, \text{pH}=7} < 10$ and $k_{\text{OH}} > 5 \times 10^9 \text{ M}^{-1} \text{s}^{-1}$				
Ibuprofen $\text{C}_{13}\text{H}_{18}\text{O}_2$		9.6	9.6	7.4×10^9
Primidone $\text{C}_{12}\text{H}_{14}\text{N}_2\text{O}_2$		<10	<10	6.7×10^9
Phenytoin $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_2$		<10	<10	6.3×10^9

^a Apparent k value for the reaction of O_3 at pH 7. ^b Species-specific k value for the reaction of O_3 with dissociated phenol or amine moiety. ^c Second order rate constant with hydroxyl radical.

In addition to the OMP's reactivity with ozone, other parameters affect the overall removal efficiency, such as the properties of the wastewater, e.g. DOM, nitrite, pH, and water temperature (Antoniou et al., 2013; Ekblad et al., 2021; Hansen et al., 2016; Zucker et al., 2015). Throughout the process of ozonation, both ozone itself and the subsequently generated $\cdot\text{OH}$ radicals play a role in eliminating OMPs (von Sonntag and von Gunten, 2012). The formation of $\cdot\text{OH}$ and ozone radicals in water along with their availability for reactions depends on the presence of other reactants such as DOM (Buffle et al., 2006) and nitrite (Mathon et al., 2021) along with the pH value of the wastewater (Elovitz et al., 2000). According to van Gijn et al. (2022), DOM is the primary factor that significantly impacts the efficiency and effectiveness of ozonation of OMPs in wastewater effluents and the impact of organic matter fractions on ozonation efficiency in wastewater effluents is often not well understood.

The main fraction of ozone is generally consumed by DOM in the wastewater matrix, primarily because it oxidizes the phenolic moieties in DOM that is found in the wastewater matrix (von Gunten, 2018). The presence of radical scavengers such as carbonate and bicarbonate along with DOM is also known to affect the performance of the ozonation. Hence, it is crucial to conduct experiments in conditions that closely resemble realistic conditions to accurately assess the removal of OMPs from municipal wastewater effluents (Vatankhah et al., 2019). Because of the limited production of $\cdot\text{OH}$ radicals from O_3 decomposition in real water matrix, along with the presence of

·OH scavengers in the water matrix, relatively high specific ozone doses such as 1 mg O₃/mg DOC are often needed for generating adequate ·OH for improving the elimination of ozone-resistant OMPs during conventional ozonation (Yao et al., 2018).

While it is challenging to alter the properties of the wastewater that enters the ozonation plant without re-designing the wastewater treatment process, it is possible to make adjustments to operational and design parameters such as the ozone dose, dispersion method, hydraulic retention time (HRT) along with coagulant addition for post-precipitation before ozonation (Ekblad et al., 2021). Optimized parameter settings such as ozone dose and HRT have been recommended to have the best treatment performance (Völker et al., 2019). Several studies have been reviewed for the removal of pharmaceuticals by ozone oxidation using different design and operation parameters (Table 1.4). It should be noted that the specific ozone dosage is not a design criteria and rather depends on the quality of the waters and the objectives of components removal, where kinetics and hydraulic considerations must be taken into account while designing an ozonation unit.

Table 1.4 : Design, system scale, operation mode, specific ozone dosage range and operation parameters for ozonation systems for removal of pharmaceuticals.

Reactor volume (m ³)	Ozone generator (country of origin)	Scale	Wastewater source	Operation mode	Specific ozone dosage (g O ₃ /g DOC)	HRT ^a in the reactor (min)	No of OMPs (Pharm)	Removal rate range (%)	Reference
25x10 ⁻⁵	Xylem GSO-30 (USA)	Bench	Spiked secondary effluent	Batch	0.27-22	1-10	17 (11)	0-100	Alameddine et al. (2021)
503 (6 reactors)	OZAT-CFV5 - Ozonia (Switzerland)	Full	Secondary effluent of WWTP	Cont.	0.35-0.97	13-43	62 (42)	21-99	Bourgin et al. (2018)
n.d.	GM2 Primozone (Sweden)	Pilot	Secondary effluent of WWTP	Cont.	0.3-0.9	10	22 (21)	0-95	Edefell et al. (2021)
0.5	GM2 Primozone (Sweden)	Pilot	Secondary effluent of WWTP	Cont.	0.2-0.8	10	20 (19)	35-95	Ekblad et al. (2021)
0.056	- (France)	Pilot	Biofiltration effluent of WWTP	Cont.	0.09-1.3	5	28 (19)	0-90	Guillossou et al. (2020)
503	OZAT-CFV5 - Ozonia (Switzerland)	Full	Secondary effluent of WWTP	Cont.	0.23-0.55	13-43	87 (70)	15-73	Gulde et al. (2021)
0.5	Primozone-GM2 (Sweden)	Pilot	Secondary effluent of WWTP	Cont.	0.18-1.3	10	TPs ^c	-	Kharel et al. (2020)
524	- (Sweden)	Full	Secondary effluent of WWTP	Cont.	0.30-0.77	10-30	TPs ^c	-	Kharel et al. (2020)
129	Effizon SMO 600 (Switzerland)	Pilot	Secondary effluent of WWTP	Cont.	0.27-1.8	20-60	70 (41)	9-99	Margot et al. (2013)
0.3	Ozone Tech Systems, ICT-10 (Sweden)	Pilot	Secondary effluent of WWTP	Cont.	0.39	65	21 (15)	23-100	Östman et al. (2019)
50	Primozone- GM48 (Sweden)	Full	Secondary effluent of WWTP	Cont.	0.55	71	21 (15)	14-100	Östman et al. (2019)
0.049	-	Pilot	MBR ^b effluent	Cont.	0.96	26.1	28 (8)	11-99	Schneider et al. (2020)
0.316	SGC 21, Pacific Ozone (USA)	Pilot	Tertiary-filtered wastewater effluent	Cont.	0.3-0.85	-	25 (13)	20-98	Vatankhah et al. (2019)
0.0094	OL80F/DST, Ozone services, (Canada)	Pilot	Secondary effluent of WWTP	Cont.	1-2	5-20	8 (7)	73-100	Yao et al. (2018)

^aHRT: Hydraulic retention time. ^bMBR: Membrane bioreactor ^cTPs: Transformation products of 7 pharmaceuticals

The removal of pharmaceuticals from wastewater effluent by ozone oxidation has been studied extensively. Edefell et al. (2021) showed that at the lowest dose of ozone, 0.3 g O₃/g DOC, ~20% of the investigated OMPs were removed beyond the limit of quantification (LOQ). Most of the investigated compounds were highly reactive with ozone such as carbamazepine, diclofenac, sulfamethoxazole, and trimethoprim. In addition to this, most OMPs were removed by over 60% at an ozone dose of 0.5 g O₃/g DOC. On the other hand, an antiepileptic drug gabapentin was removed less than 50% at 0.5 g O₃ /g DOC and required a higher ozone dose for improved removal. Bourgin et al. (2018) investigated the removal of OMPs and the formation of oxidation by-products via ozonation in a full-scale WWTP. The study revealed that a specific ozone dose of 0.55 g O₃/g DOC was effective in ensuring an average abatement of the twelve selected indicator substances by 80% over the whole treatment chain in the WWTP, where this dose was very efficient in abating a broad range of OMPs by on average >79%. Issaka et al. (2022) reviewed advanced catalytic ozonation for the degradation of pharmaceuticals, where the treatment efficiency of advanced catalytic ozonation for pharmaceuticals has been summarized within the scope of current challenges, problems and prospective research directions. According to the study by Östman et al. (2019), the conventional treatment (13,000 person equivalent (PE)) with the add-on of full-scale ozonation (0.55 g O₃/g TOC) has achieved ~90% removal for most of the studied compounds, not including benzotriazoles and fluconazole (~50%).

The impact of the treatment system scale on the removal of pharmaceuticals in the wastewater via ozone should be considered while comparing similar studies in Table 4. Since the laboratory-scale studies tend to optimize the conditions that favor the removal efficiency of the compounds, pilot- or full-scale studies often result in lower compound removal rates. For instance, Alameddine et al. (2021) studied the removal of atrazine and carbamazepine in a laboratory-scale study, by spiking the compounds into the wastewater in high concentrations in order to avoid possible interference from other wastewater contaminants. In addition, the impact of other parameters such as DOM in the wastewater is often not tested in the laboratory-scale, whereas studies in pilot- or full-scale treatment plants (Ekblad et al., 2021), in which the effect of wastewater characteristics was investigated on the removal of micropollutants, present more realistic results.

1.3.2.2 Formation of transformation products

OMPs including pharmaceuticals are usually not mineralized but instead converted into smaller compounds called ozonation transformation products which are often more biodegradable and less toxic (Hübner et al., 2015; Völker et al., 2019), but can be also more toxic than the parent compound (Zilberman et al., 2023). In principle, with a comprehensive understanding of the reaction mechanisms and reaction rates of a substance or its components with ozone, it is possible to predict the potential ozonation transformation products and assess the substance's removal rate, which can be achieved through the application of high-resolution mass spectrometry for screening (Hübner et al., 2015; Lee and von Gunten, 2016; von Sonntag and von Gunten, 2012). Although mechanistic information is usually available, there are still major knowledge gaps on the degradation pathways of pharmaceuticals (Bourgin et al., 2018).

Several researchers have studied the formation or the removal of ozonation transformation products (Gulde et al, 2021; Kharel et al, 2020). In the study of Gulde et al. (2021), from 87 selected OMPs (mainly pharmaceuticals and pesticides), 84 ozonation transformation products from 40 different OMPs were identified during the ozonation of secondary wastewater effluent from 4 different WWTPs, where the specific ozone doses ranged between 0.23 and 0.55 g O₃/g DOC. Kharel et al. (2020) investigated the dependence of ozone dose for the formation and removal of ozonation pharmaceutical transformation products in pilot- and full-scale municipal WWTPs. According to the results of this study, the ozone reactivity of all metabolites (ozone dose which removes 90% of the compound is called decadic ozone dose) was lower than those of their parent compounds. For epoxy-carbamazepine, di-OH-carbamazepine and N-desmethyl tramadol, the decadic ozone dose was 1.0, 1.3 and 1.1 mg O₃/mg DOC, respectively.

Bourgin et al. (2018) studied the transformation products and oxidation by-products in a full-scale WWTP upgraded with ozonation and biological post-treatments. According to Bourgin et al. (2018), the formation of bromate and *N*-nitrosodimethylamine (NDMA) during ozonation needs to be assessed since these by-products are known to be potentially carcinogenic and toxic. Another ozonation by-product, bromate emerges through a sequence of oxidative reactions of bromide that are present in water bodies and wastewaters in µg/L-mg/L levels, whereas NDMA is

generated when precursors such as hydrazines and sulfamides undergo ozonation (Bourgin et al., 2018).

Edefell et al. (2021) studied the degradation of transformation products and ozone-resistant OMPs from biologically treated wastewater. The study combined the ozonation with a moving bed biofilm reactor (MBBR) in pilot-scale system which was operated for 16 months. This study revealed that the N-oxides which were formed during ozonation from erythromycin, clarithromycin, tramadol, and venlafaxine could not be degraded by the biofilm. The formation of N-oxides increased by 20% to 80% compared to the influent concentration of the parent compounds at an ozone dose of 0.5 g O₃/g DOC, where N-oxides were the main transformation products of the tertiary amines. To address the issues posed by by-products such as nitrosamines and potentially the transformation products resulting from ozonation, a biological or physical post-treatment step is often recommended such as fixed bed bioreactors, GAC filters, and moving bed biofilm reactors, which can help to alleviate the detrimental impacts in receiving water bodies.

1.3.3 Carbon-based filter/filling materials

The adsorption process is not characterized by a single factor; instead, it involves a multitude of physical and chemical interactions among OMPs, activated carbon and dissolved organic matter (Guillossou et al., 2019; Mailler et al., 2016; Margot et al., 2013). Typically, the breakthrough pattern for each OMP is contingent upon its chemical attributes, encompassing factors like hydrophobicity (often expressed as K_{ow}), aromaticity, molecular size, the extent of competition with other OMPs and dissolved organic matter (DOM) (Altmann et al., 2016). Compounds that possess elevated log K_{ow} values (indicating high hydrophobicity) and contain aromatic structures, such as carbamazepine and diclofenac, generally exhibit superior adsorption onto the activated carbon surface compared to compounds with greater hydrophilicity such as sulfamethoxazole (Kovalova et al., 2013). On the contrary, a research conducted by Guillossou et al. (2019) found that there was no discernible pattern in the removal of OMPs by GAC in relation to their physical and chemical characteristics, including size, charge, polarizability or specific functional groups.

The adsorption capacity of the activated carbon decreases over time due to saturation in the adsorber surface which is also referred as the breakthrough point. Altmann et al.

(2016) studied the breakthrough curves of 15 OMPs, where all OMPs were completely retained at the beginning of GAC filtration and normalized concentrations subsequently increased depending on the adsorbability of each compound. In the same study, effluent concentrations of diatrizoic acid and acesulfame increased to almost 1.5 times of the influent concentration, showing that previously adsorbed substances were desorbed, which is attributed to the competition with well-adsorbing compounds resulted in desorption after complete breakthrough. In the study by Bourgin et al. (2018), a significant difference in the breakthrough of the compounds was observed, where compounds such as diclofenac, venlafaxine, metoprolol and hydrochlorothiazide demonstrated a much later breakthrough compared to the other compounds (acesulfame, sucralose, candesartan, benzotriazole) with weaker sorption behavior.

The removal efficiency of the pharmaceuticals greatly depends on the wastewater characteristics, where the DOM in the wastewater has an important impact on the removal. Competition between the DOM and the OMPs can occur in the treatment processes such as oxidation and adsorption. Altmann et al. (2016) pointed out that high DOC and suspended solids concentrations in the influent of the GAC adsorber greatly limit the process, which might result in frequent backwashing and unsatisfactory filtration efficiency. High DOC concentrations are usually seen as a drawback for the adsorption of OMPs onto GAC since long-term carbon fouling reduces the adsorption capacity and leads to accelerated breakthrough (Altmann et al., 2016). In a study by Guillosoy et al. (2019), the low removal of erythromycin and roxithromycin by GAC was attributed to their molecular size since large molecules could not access micropores but only to mesopores where a higher competition with the DOM occurred. In addition, a good correlation between UV_{254} and OMP removal via GAC along with a good correlation between DOC and micropollutant removal has recently been highlighted in the literature at laboratory- and pilot-scale (Mailler et al., 2016; Altmann et al., 2014).

Removal of pharmaceuticals via activated carbon has been studied extensively by using both GAC and PAC. In one study by Kårelid et al. (2017), GAC and PAC were compared for the removal of pharmaceuticals from wastewater on pilot-scale. According to the study, the PAC system achieved a 95% removal efficiency by applying a fresh dose of 15-20 mg/L, where carbon utilization rates for the GAC

application had a much broader range from <28 to 230 mg/L contingent upon the type of carbon product. It was emphasized that if the main aim was to maximize the removal efficiency of pharmaceuticals in the wastewater, Kårelid et al. (2017) recommended to use of PAC, whereas in terms of carbon usage and practicability, GAC is often the better alternative.

1.3.3.1 Granular activated carbon (GAC)

Removal of pharmaceuticals by activated carbon has been studied previously worldwide (Vatankhah et al., 2020; Bourgin et al., 2018; Östman et al., 2019; Altmann et al., 2016; Benstoem et al., 2017; Guillosoy et al., 2019). Examples from the current literature in terms of pharmaceutical removal by GAC using column reactors including the empty bed contact time (EBCT) and treated bed volume (BV) are presented in Table 1.5. The removal of OMPs greatly depends on the operation time of the GAC system, where the breakthrough for each compound depends on their physicochemical properties and the quality of the wastewater.

Table 1.5 : Design and operation parameters for removal of OMPs including pharmaceuticals using GAC systems.

Scale	Reactor height (m) - volume (m ³)	GAC type (origin)	Operation mode	Flowrate (L/h)	EBCT ^a (min)	Bed volume	No. of OMPs	Removal (%)	Reference
Pilot	4 – 0.07	Epibon A 8x30 mesh (Germany)	Upflow	105	19	3000-25000	15	0-100	Altmann et al. (2016)
Pilot	n.g. -77	Cyclecarb 401 (Belgium)	Upflow	300	14.5	10000-28000	51	>80	Bourgin et al. (2018)
Pilot	5 – 12	CycleCarb 305 (Belgium)	Upflow	33x10 ³	20	-	48	13-98	Guillosoy et al. (2019)
Pilot	5 – 20	Cyclecarb 305 (Belgium)	Upflow	58.3 x10 ³	10-20	-	57	25-90	Mailler et al. (2016)
Pilot	2 – 0.036	Filtrisorb 300 (USA)	Upflow	61.2	-	7310-14620	21	99	Östman et al. (2019)
Pilot	4.0 – 0.072	Filtrisorb 400 (USA)	Upflow	300	30	-	13	3-56	Vatankhah et al. (2019)

^a EBCT = Empty bed contact time

Benstoem and colleagues (2017) conducted a systematic review of existing literature and identified 44 studies that examined the adsorption of OMPs (namely carbamazepine, diclofenac and sulfamethoxazole) from municipal wastewater using GAC at both pilot and full-scale levels. A pilot-scale study by Altmann et al. (2016) explored the integration of GAC adsorption and deep-bed filtration with coagulation

into a single advanced treatment process to simultaneously eliminate OMPs and phosphorus from secondary effluent. Results indicated that OMPs with high adsorption potential (e.g. benzotriazole, carbamazepine) were eliminated by >80% after 8000-10,000 BV, while OMPs that are weakly to medium adsorbing such as primidone and sulfamethoxazole showed removals <80% at <5,000 BV. Another pilot study by Guillosoy et al. (2019) showed substantial elimination for 11 pharmaceuticals (atenolol, azithromycin, carbamazepine, citalopram, diclofenac, hydrochlorothiazide, ketoprofen, naproxen, ofloxacin, oxazepam, tetracycline) with average removals ranging from 50 to 80%. In the same study, compounds such as erythromycin, irbesartan, lorazepam, roxithromycin, sulfadiazine and sulfamethoxazole had low removal efficiencies ranging from 30% to 50%.

Vatankhah et al. (2019) studied the removal of 13 OMPs in a pilot-scale setup, where the highest removal rate was observed for naproxen, trimethoprim, and gemfibrozil (43%, 50%, and 56%, respectively), while sucralose, tris (2-carboxylethyl) phosphine and N-nitrosomorpholine showed approximately 13%, 18%, and 19% removal, respectively, with 2.0 g GAC/L. Bourgin et al. (2018) focused on the abatement of OMPs, which were run for 28000 BV that corresponds to 10 months of operation. The results showed >80% removal of diclofenac, metoprolol, venlafaxine and hydrochlorothiazide (group I, see Table 3) and >50% acesulfame, sucralose, candesartan, benzotriazole (group II) after 8000 BV. After 28000 BV, group I and group II compounds were abated >40% and >20%, respectively. Similarly, a study by Östman et al. (2019) revealed that the average elimination of all compounds via one of the tested GACs was ~99%, whereas the least efficient GAC removed the OMPs by ~68% on average. Mailler et al. (2016) studied μ GAC for the first time in the literature. Results indicated that pharmaceuticals had a good affinity for μ GAC and showed high (~60%) or very high (~80%) removals for most of the quantified compounds ($n=22$ and 32, respectively), such as atenolol (92–97%), carbamazepine (80–94%), ciprofloxacin (75–95%), diclofenac (71–97%), oxazepam (74–91%) or sulfamethoxazole (56–83%).

The fate of pharmaceutical transformation products in the GAC system has also been studied by several researchers. In the study of Altmann et al. (2016), the effluent concentration of sulfamethoxazole exceeded the influent concentration after a complete breakthrough at ~8,000 BV, which was explained by the formation of

sulfamethoxazole in the GAC filter due to back-transformation of metabolites. Bourgin et al. (2018) studied the fate of selected ozonation transformation products during GAC treatment, where the removal was ~80% for N-oxides (clarithromycin N-oxide, tramadol N-oxide, venlafaxine N-oxide and fexofenadine-N-oxide) and even >96% for chlorothiazide after ~80000 BV. Subsequently, the elimination of the N-oxides started to decline, but stayed above 80% until 170000 BV for chlorothiazide. At 230000 BV, the removal of N-oxides was <40%, while chlorothiazide abatement was still higher (57%). Knopp et al. (2016) discovered that even though 11 of the chosen OMPs were still detectable following the ozonation, the majority of them were successfully removed during the subsequent GAC filtration at ~25,000 BV. Furthermore, ozonation of the analgesic tramadol resulted in the formation of tramadol-N-oxide which was effectively eliminated by GAC filters.

1.3.3.2 Powdered activated carbon (PAC)

Several studies have focused on PAC for the removal of OMPs including pharmaceuticals from wastewater. Margot et al. (2013) studied the removal of 70 OMPs including pharmaceuticals via PAC, where compounds were removed >80% on average compared with raw wastewater, with a PAC dose between 10 and 20 mg/L. The research findings indicated that when dealing with delicate receiving waters such as drinking water sources or recreational waters, the combination of PAC treatment with ultrafiltration (UF), despite its present higher expense, emerged as the most appropriate choice. This combination allowed for the effective removal of most OMPs and macropollutants, without generating the problematic by-products, resulting in the most significant reduction in toxicity and complete disinfection of the effluent. Another study that focused on PAC for the removal of OMPs showed that the removals were all below 30% at a PAC dose of 2 mg/L for 10 OMPs, while the removal remained between 10 and 30%, except for diuron (42%) and propranolol (43%), using 5 mg/L of PAC (Guillossou et al., 2020).

Delgado et al. (2022) studied a novel configuration with PAC for the removal of two recalcitrant pharmaceuticals (carbamazepine and sildenafil) via fixed bed filters which was operated in down-flow mode (downward flow). The laboratory-scale study revealed that the sildenafil was efficiently removed, while the carbamazepine reached saturation after 25 days of continuous operation, defining it as the limiting pollutant.

Furthermore, a pilot plant using PAC with a total bed height, PAC mass, contact time, surface rate and working flow of 20 cm, 40 g, 40 min, $0.4 \text{ cm}^3/(\text{cm}^2 \text{ min})$ and 30 mL/min, respectively, achieved removal efficiencies above 90%.

1.3.3.3 Biochar

Biochars are carbon-rich substances created through the pyrolysis of biomass, encompassing materials like agricultural and forestry residues, sludge and other organic matter. Biochar is considered as a promising substitute for activated carbon in adsorption applications due to its sustainability as a material and its exceptional physicochemical properties, which include high specific surface areas, large pore volumes and abundant functional groups (Shin et al., 2020). Employing biochar can provide an effective means of enhancing waste management practices since the conversion of biomass waste into valuable products such as adsorbents and syngas can help mitigate the pollution of water bodies, soil and the atmosphere while also reducing greenhouse gas emissions (Chu et al., 2019). It's worth noting that the activated products resulting from the biomass pyrolysis process often exhibit lower surface areas and pore volumes compared to traditional activated carbon. This limitation may pose challenges in the practical use of biochar for water and wastewater treatment applications (Shin et al., 2020). However, this issue might be solved by chemical modification techniques (such as alkali, acid or oxidative modified biochars), where these techniques allow the potential to generate biochars with greater surface areas, better porous structures and lower ash contents compared to commercialized activated carbon (Chu et al., 2019).

Biochar is considered as a great alternative in terms of removal of OMPs from wastewater including pharmaceuticals (Hagemann et al., 2020). Biochars that are used for the treatment of OMPs in wastewater might be produced from different sustainable materials such as wood, biomass, solid waste, coffee grounds, sewage sludge and other materials (Li et al., 2022; Hagemann et al., 2020; Shin et al., 2020). Although pharmaceuticals are an emerging class of OMPs in wastewater, there have been limited recent investigations that have examined the adsorption and elimination of pharmaceuticals from wastewater using biochars (Ouyang et al., 2020). Ihsanullah et al. (2022) reviewed the removal of pharmaceuticals from water using sewage sludge-derived biochar, where the removal of various pharmaceuticals by sludge-based

biochar has been described in detail, with the primary focus has been on elucidating the adsorption mechanism and their reusability potential. One of the key findings of the review paper was that continuous flow experiments at bench-scale were required to better evaluate the potential of biochar in practical applications, while it was emphasized that further research is required to evaluate the viability of utilizing biochar in practical water treatment scenarios, taking into account the complexities of natural environmental conditions and the presence of other pollutants. Xiang et al. (2020) reviewed the biochar technology in wastewater treatment, where the effectiveness of the biochar in terms of OMPs removal was considered as closely related to the aromaticity index, polarity index, specific surface area and the quantity of oxygen functional groups. According to a study by Li et al. (2022), OMPs are prone to be adsorbed on municipal solid waste derived biochar due to the well-developed micropores and abundant functional groups. In a study by Yao et al. (2018), it was revealed that the sulfamethoxazole adsorption onto the digested bagasse biochars was mainly controlled by π - π interaction and affected by the solution pH value.

Hagemann et al. (2020) studied wood-based activated biochar to remove 15 model OMPs including pharmaceuticals such as diclofenac, clarithromycin, citalopram, carbamazepine, irbesartan, metoprolol, sulfamethoxazole and venlafaxine, where at circumneutral pH a removal was achieved to the same or higher extent than commercial activated carbon that was used as a reference. Shin et al. (2020) investigated the single and competitive adsorption characteristics of OMPs using the pristine and alkali-modified spent coffee grounds (SCG) biochar. According to the research findings, both the individual and competitive adsorptions of the OMPs were significantly influenced by the solution's pH and ionic strength. This was primarily due to the dominant factors of pore-filling effects, electrostatic interactions, and hydrophobic interactions governing their removal when using both pristine and alkali-modified SCG biochars. The higher removal efficiencies of the OMPs by the alkali-modified SCG biochars ($\geq 45\%$) in the presence of DOM compared to the pristine SCG biochars ($\leq 19\%$) were observed. Sun et al. (2018) studied the removal of sulfonamide antibiotics including sulfamethoxazole, sulfadiazine, sulfamethazine, sulfadimethoxine, and one human metabolite (N_4 -acetyl-sulfamethoxazole) by biochar and biochar/ H_2O_2 in synthetic urine, where except N_4 -acetyl-sulfamethoxazole, all the parent sulfonamides were degraded in urine matrix. Pedrosa et al. (2022) studied a

Spirulina-based carbon bio-sorbent, which removed in less than 30 min more than 88% of most studied 20 OMPs belonging to 5 classes (6 antibiotics, 3 beta-blockers, 5 multi-class pharmaceuticals, 4 herbicides, and 2 insecticides) that were spiked at 100 µg/L each in a secondary effluent sample of a municipal WWTP.

1.3.4 Other sorption systems

1.3.4.1 Ion exchange (AIX)

Numerous reaction mechanisms contribute to the adsorption of OMPs onto AIX (Michael-Kordatou et al., 2015). The majority of pharmaceuticals are classified as weak organic acids or bases, a characteristic that enhances their adsorption onto oppositely charged polymers like AIX, making it even more effective than adsorption onto activated carbon (Bäuerlein et al., 2012). On the other hand, other molecular level bonds also contribute to the removal process. For instance, the substantial removal of diclofenac by AIX was ascribed to a blend of factors, including Coulombic interactions, van der Waals forces between the polystyrenic resin structure and the benzene rings of diclofenac, and potentially hydrogen bonding involving the dimethylethanol amine functional group's side chain and the carboxylate and amine functional groups found in diclofenac (Landry and Boyer, 2013). Wang et al. (2016) studied the removal mechanism of pharmaceuticals by AIX resins over long-term (eight adsorption-regeneration cycles), where the removal of 12 selected pharmaceuticals was investigated for the effect of resin charged functional group, porosity, and chemical matrix. Numerous studies have underscored the significant capacity of commercially available AIX to effectively eliminate pharmaceuticals from diverse water sources (Table 1.6).

In a study by Tang et al. (2021), the negatively charged species of sulfamethoxazole, sulfamerazine, bezafibrate, gemfibrozil, naproxen and ibuprofen could be effectively removed from the secondary effluent by AIX, with maximum removal efficiencies between 31 and 63% at a magnetic ion-exchange resin (MIEX)[®] dosage of 8 mL/L. The same study revealed that the zwitterion-rich OMPs, including chlortetracycline, oxytetracycline, enrofloxacin, norfloxacin and caffeine can be removed through both electrostatic and non-electrostatic interactions, with removal efficiencies between 23 and 50%. On the other hand, the non-ionic OMP removal efficiencies of MIEX[®] were

low with 21% and 13% for the neutral molecules of carbamazepine and atrazine at pH 7.5 ± 1 , respectively.

Table 1.6 : Overview of commercial AIX to remove pharmaceuticals from various water matrices.

AIX resin type	Target compounds	Scale	Operation mode	Matrices	Dosage (mL/L)	Removal rate (%)	Reference
Oasis MAX resin	Caffeine and metformin	Laboratory	Continuous	Spiked water	-	-	Bäuerlein et al. (2012)
MIEX® resins	7 sulfonamide antibiotics, 7 tetracyclic antibiotics	Laboratory	Batch	Treated drinking water	0.5-5	15-90	Choi et al. (2007)
Purolite A520E, Dowex 22, Dowex Marathon 11Amberlite IRA958	Diclofenac	Laboratory	Batch	Synthetic human urine	8	40-100	Landry and Boyer (2013)
Dowex 22 resins	Diclofenac, ketoprofen, and naproxen, ibuprofen, paracetamol	Laboratory	Continuous	Synthetic human urine	1-16	14-95	Landry et al. (2015)
MIEX® resins	13 selected pharmaceuticals	Laboratory	Batch	Spiked secondary effluent	8	13-63	Tang et al. (2021)
D201, D001, D4006, 201x4 and 213 resins	12 pharmaceuticals	Laboratory	Continuous	Synthetic wastewater	4.2	0-100	Wang et al. (2016)

1.3.4.2 Constructed wetlands

A constructed wetland is a nature-based water treatment technology, which can be used to remove OMPs from WWTP effluent. Few studies exist in the literature that utilize constructed wetlands to remove OMPs. Lei et al. (2023) studied the removal of OMPs from treated effluent by batch-operated pilot-scale constructed wetlands. Results revealed that the use of bark-biochar as a support matrix increased the removal of 11 of 12 studied OMPs compared to the constructed wetlands filled with conventional material sand. The inclusion of bark-derived biochar resulted in removal rates exceeding 40% for irbesartan, carbamazepine, hydrochlorothiazide, and benzotriazole in the aforementioned study. Another study by Venditti et al. (2022) focused on the removal of 27 selected OMPs in vertical flow constructed wetlands as post-treatment for municipal wastewater, where six substrates (i.e. sand enriched with activated or non-activated biochar or zeolite in different ratios) were tested. According to the results of the study, constructed wetlands with 15% activated biochar mixed with sand proved to be effective in the removal of 18 OMPs and complied with national discharge standards for 4 selected compounds. Matamoros et al. (2008) studied the

OMP removal in a full-scale surface flow constructed wetland fed with secondary effluent, where the removal efficiencies were consistently above 90% for all compounds, except for carbamazepine and clofibric acid, which exhibited removal rates ranging from 30% to 47%.

1.3.4.3 Biofiltration

Biofiltration systems consist of a support material such as sand or activated carbon to create a biofilm on the surface of the material and support the biological activity in a filtration unit. The most common biofiltration technologies are sand filtration, biological activated carbon (BAC) filtration, riverbank filtration and managed aquifer recharge (Reungoat et al. 2011). Reungoat et al. (2011) investigated the biofiltration for the removal of DOC, pharmaceuticals and personal care products (PPCPs) from real wastewater in a pilot scale, where two filtering media (sand and GAC) were tested. The results of the study showed that BAC has a good potential for the removal of DOC (35-60%) and PPCPs (>90%) even without pre-ozonation, while the sand showed limited improvement in effluent quality. Müller et al. (2017) investigated the removal of diclofenac, carbamazepine, metoprolol and benzotriazole from the wastewater treatment plant effluent via sequential biofiltration (SBF). According to the results of this study, an increased removal of the compounds was observed in an SBF system as compared to a conventional single-stage biofiltration unit operated at the same overall EBCT.

The combination of a BAC filter coupled with an ultrafiltration (UF) unit was evaluated by Sbardella et al. (2018) as an advanced treatment for pharmaceutically active compounds removal at pilot-scale. In the same study, a laboratory-scale system was operated for four months to quantitatively assess the contributions of adsorption and biodegradation. The results underscored the crucial role played by GAC within the biofiltration units. Specifically, it was observed that the biofilm contributed to the removal of approximately 22%, 25%, 30%, 32%, and 35% of ciprofloxacin, bezafibrate, ofloxacin, azithromycin, and sulfamethoxazole, respectively.

1.3.5 Combination of ozone with sorption filtration systems

1.3.5.1 Ozone with GAC

Bourgin et al. (2018) evaluated a full-scale WWTP upgraded with ozonation and biological and adsorptive post-treatments for the abatement of OMPs and formation of transformation products. 240 of 550 investigated OMPs were pharmaceuticals, of which 43 of them were evaluated for biological treatment along with the ozonation removal rates (0.35-0.97 g O₃/g DOC). According to the results, substances with high reactivity with ozone including diclofenac, carbamazepine, hydrochlorothiazide, sulfamethoxazole and tertiary amines (e.g. cetirizine, fexofenadine and tramadol), had high removal rates (>80%) at circumneutral pH even at 0.35 g O₃/g DOC. Moreover, three different biological treatments (sand filtration, moving bed, fixed bed) and GAC filtration (both fresh and preloaded) were assessed as subsequent treatments following the ozonation process. The fresh activated carbon filtration led to a substantial increase in the removal of OMPs after ozonation, primarily because of its sorption capabilities. The reduction of the indicator substances varied from 20% to 89% after 270,000 BV and remained significant even after reaching 500,000 BV.

Kharel et al. (2021) conducted research aimed at clarifying the elimination of pharmaceutical human and microbial metabolites based on the specific ozone dosage. They applied ozonation to four locations, including two pilot-scale and two full-scale plants situated downstream of conventional activated sludge plants. The specific ozone dosage (nitrite corrected) in the pilot- and full-scale treatment plants ranged between 0.1-1.7 mg O₃/mg DOC. The metabolites exhibited lower reactivity with ozone compared to the parent compounds. In the same study, it was found that GAC outperformed BAC, anthracite, and constructed wetlands in terms of effectiveness as a polishing step for the removal of compounds. Östman et al. (2019) presented the effect of full-scale ozonation and pilot-scale GAC on the removal of biocides, antimycotics and antibiotics in a WWTP which had the first full-scale ozonation system in Sweden. Ozone (0.55 g O₃/g total organic carbon (TOC)) was not effective in removing the benzotriazoles and fluconazole, whereas high removal efficiency (>99%) of 2-(methylthio)-benzothiazole was obtained by utilizing GAC filtration.

Vatankhah et al. (2019) investigated the removal of a wide range of OMPs including pharmaceuticals from the municipal wastewater effluent by using simultaneous ozone

and GAC treatment. The study's findings indicated that the removal of tris (2-carboxylethyl) phosphine (TCEP), sucralose and meprobamate was improved in the O₃/GAC treatment trials when compared to the combined removal observed in separate ozonation and GAC adsorption experiments. Additionally, the investigation unveiled that the extended O₃/GAC trial demonstrated a significant decline in the enhancing impact of GAC after 20 hours of ozone exposure, where the decline was found to be associated with alterations in the surface properties of GAC caused by ozone.

1.3.5.2 Ozone with PAC

Alameddine et al. (2021) studied PAC-catalyzed ozonation of pharmaceuticals, where carbamazepine and atrazine were used as surrogate OMPs. Results of the study indicated that the PAC-catalyzed ozonation improved the removal of OMPs in primary effluent. Results indicated that the high reactive compounds such as carbamazepine, sulfamethoxazole and naproxen were removed 80-100% with ozonation of 0.27 g O₃/g DOC with the addition of 100 mg PAC/L increased the overall removal slightly. Other pharmaceuticals such as ibuprofen and fluconazole, which have intermediate-low interaction with ozonation, had <50% removal with 2.2 g O₃/g DOC which increased to 50-80% with the addition of 100 mg PAC/L.

Guilloso et al. (2020) studied the removal of 28 OMPs (19 pharmaceuticals, 6 pesticides, 2 hormones and 1 perfluoroalkyl sulfonic acid) to assess the advantages of ozonation before PAC adsorption for the treatment of municipal wastewater. In this research, the effect of ozonation (0.09, 0.22, 0.94 and 1.29 g O₃/g DOC) on OMP adsorption was assessed, where OMP adsorption was not changed at low specific ozone (<0.30 g O₃/g DOC) doses but increased at higher specific ozone doses (>0.90 g O₃/g DOC) related to the decrease in the adsorption of DOM and competition with OMPs. The study also suggested the correction of the specific ozone dose according to the suspended solids levels, in addition to nitrite. Loganathan et al. (2022) reviewed the ozonation/adsorption hybrid treatment system for improved removal of DOM and OMPs from drinking water. According to the study, ozonation causes a conversion of larger DOM molecules into smaller ones with reduced aromatic and hydrophobic characteristics, where this transformation leads to a decrease in their ability to be

adsorbed. Consequently, the reduced adsorption of these molecules reduces their competition with OMP adsorption, ultimately enhancing the removal of OMPs.

1.3.5.3 Ozone with other sorption systems

Although the combination of ozone with AIX resins is not well investigated in the literature, the hybrid process might be promising in terms of pharmaceutical removal from the wastewater. In a study by Tang et al. (2021), the removal characteristics including bulk organic indicators, OMPs, bio-toxicity, and fluorescence were compared using MIEX[®], ozonation, and the hybrid process of MIEX[®] followed by ozonation in the secondary effluent. Results indicated that the removal of selected pharmaceuticals (such as naproxen, ibuprofen, atrazine, sulfamethoxazole, carbamazepine and gemfibrozil) via MIEX[®]-O₃ combination was 75-99%. Additionally, the combination process (MIEX[®] and ozonation) was capable of removing more organic matter in the effluent wastewater than the individual MIEX[®] or ozonation processes and could decrease the genotoxicity and oestrogenic activity under the limit of detection.

Fu et al. (2022) investigated the elimination of OMPs from wastewater effluent using a selective adsorption approach involving a fixed-bed granular zeolite filter, followed by an in-situ regeneration process based on ozone. The study reported removal efficiencies for eight OMPs (namely, sotalol, metoprolol, propranolol, trimethoprim, clarithromycin, carbamazepine, methyl-benzotriazole, and benzotriazole) in the range of 70% to 100% using 8 mg/L ozone dosage via zeolite adsorption and ozone-based regeneration. The research findings demonstrated that utilizing ozone gas directly in ozonation can efficiently regenerate the zeolite granules within the column, all while keeping ozone consumption at a minimum level.

There are few studies regarding the combination of ozone with constructed wetlands for the removal of pharmaceuticals in wastewater. Lancheros et al. (2019) investigated the elimination of ibuprofen and naproxen from household wastewater by integrating ozonation with a horizontal subsurface flow constructed wetland. Results of the study revealed that using the medium ozone dose (15 mg/L) combined with the constructed wetland, overall removal efficiency was on average 97% and $\geq 97\%$ for ibuprofen and naproxen, respectively.

Lee et al. (2012) conducted a pilot-scale research study exploring the elimination of PPCPs and other OMPs from treated wastewater, where they employed a combination of ozone and biofiltration as an alternative to reverse osmosis (RO). It was suggested that biofiltration should be employed to treat the effluent from the ozone contactor to reduce the occurrence of unknown byproducts resulting from the oxidation of micropollutants in the treated water. Another study by Piras et al. (2020) included granular biofiltration for controlling micropollutants in tertiary treated municipal wastewater for potable reuse applications, where the treatment sequence, which combines two advanced oxidation processes (AOPs) with granular biofiltration using activated carbon ($O_3/H_2O_2 + BAC + UV_{254}/H_2O_2$), demonstrated remarkable effectiveness, achieving a remarkable 99% reduction in total OMPs.

1.3.6 Fate of transformation products after sorption systems

According to Guillosoou et al. (2020), to mitigate the presence of transformation products and oxidation by-products, an extra treatment stage such as sand filtration or the use of activated carbon filters was necessary following the ozonation process. Schneider et al. (2020) worked on the toxicity removal by ozone coupled with activated carbon/biofiltration using both pilot- and full-scale systems. According to the study by Schneider et al. (2020), ozonation largely removed estrogenic and anti-androgenic activity, while anti-estrogenic and mutagenic effects increased suggesting the formation of toxic transformation products. The same study showed that these effects were significantly reduced by GAC being more effective than biological filtration. Therefore, ozonation coupled with GAC filtration seemed one of the most promising treatment processes in terms of reducing the toxicity.

According to Gulde et al. (2021), the overall abatement of the transformation products in the various post-treatments was low in biological sand filtration, whereas the removal was better using GAC columns (higher BVs resulted in decreased efficiency), and best using PAC treatment. Völker et al. (2019) performed a review that focused on the removal of toxicity using ozonation and activated carbon, where their findings highlighted that upgrading to either ozonation or activated carbon treatment would considerably enhance the removal of toxicity in WWTPs. The study highlighted that Ozonation produces harmful transformation byproducts that can be eliminated through a subsequent treatment process.

2. MATERIAL AND METHODS

2.1 Experimental Setup

The experimental set-up consisted of a continuous ozonation system followed by media filtration utilizing single filter columns with GAC, AIX, biochar 1 and biochar 2, respectively (Figure 2.1). In addition, an empty reference column was used for process control and verification. The complete set-up was protected against UV-light to prevent biological activity. The operation time per investigated O_3 -dosage was two weeks. The sampling was performed at the end of the first 24-hours, at the end of the first week and at the end of the second week. The sampling points were according to Figure 2.1 (i) wastewater container (WWTP effluent, (2)), (ii) equalization tank after ozonation (6), and (iii) column outlets of GAC (9), AIX (10), reference column (11), biochar 1 (12) and biochar 2 (13). While sampling downstream, relevant time delay was assured to catch the same water plume. Operation time at each dose was at least 10 hydraulic retention times (HRT) before sampling.

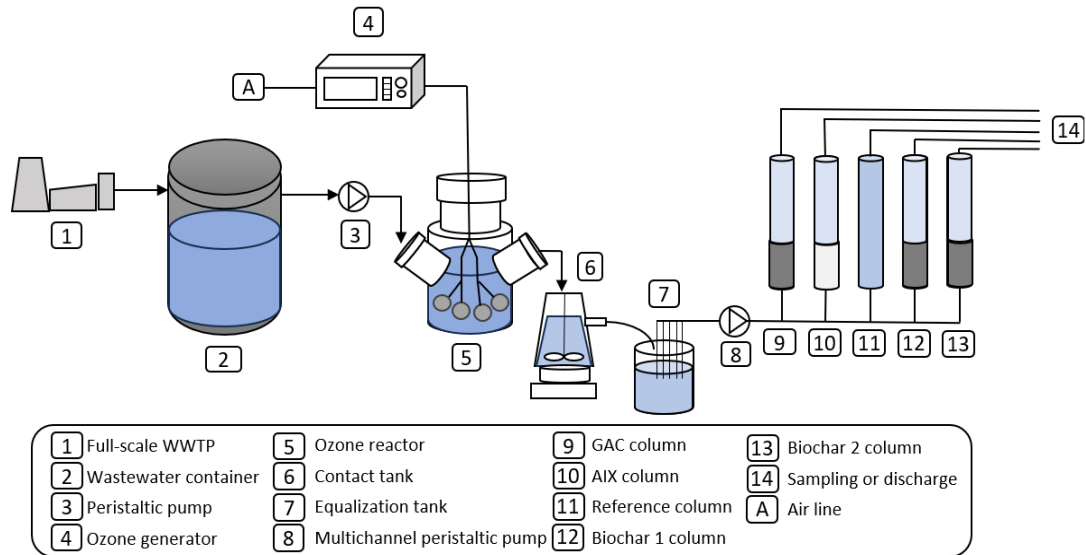


Figure 2.1 : System configuration of laboratory scale ozonation system combined with a) GAC (#9), b) AIX (#10), c) biochar 1 (#12), and d) biochar 2 (#13).

2.1.1 Ozonation system

The ozonation system consisted of an O₃-generator, reactor, contact tank and equalization tank (Figure 2.2). All tubings and equipment that might be in contact with O₃ were non-reactive with O₃ such as neoprene tubings and the glass reactor. The O₃-generator (Triogen LAB2B, UK), had an output of 0.2 to 4.0 g/hr with air as the feed gas (feed gas flow rate: 4-10 L/min). Since the O₃-production was higher than desired with the existing O₃-generator, the O₃-line was bypassed via a stainless steel T valve in order to achieve the desired three different low O₃-production rates (4, 8 and 12 mg/L O₃). The O₃ dosage was monitored via wet analysis (iodometric method) within reasonable time intervals (at least each operation day). The operation time of each O₃ dosage was two weeks, and the O₃-contact time was approximately 15 min for each operational condition.

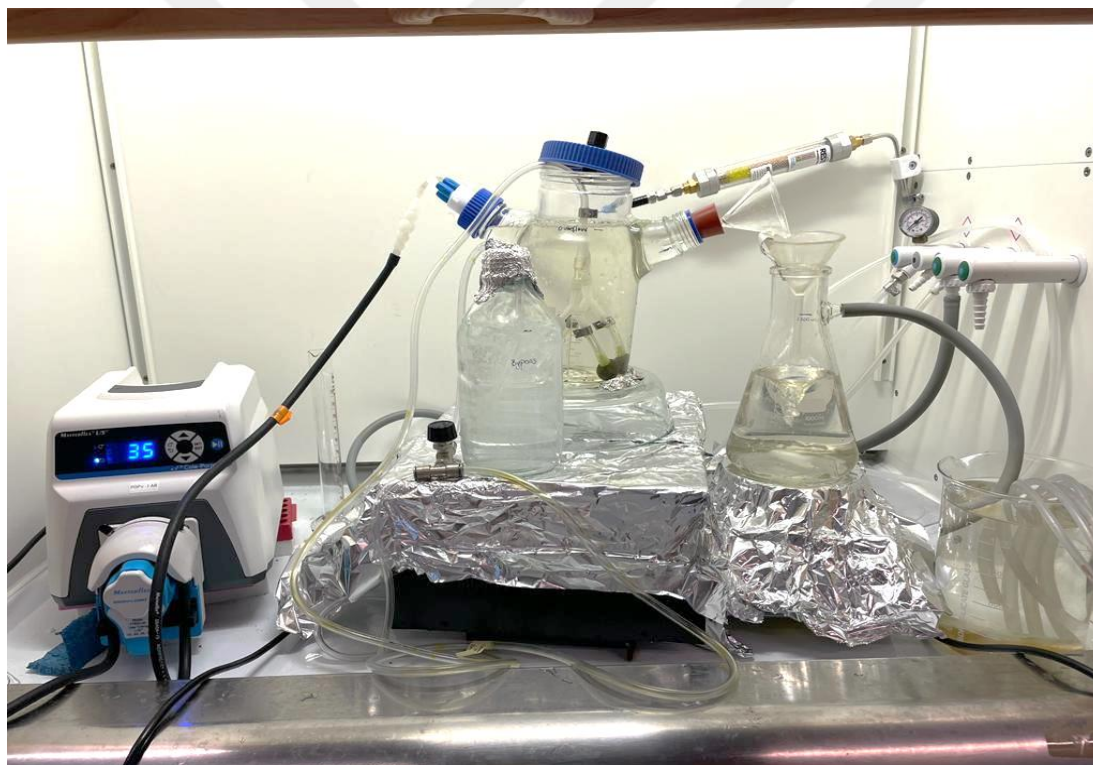


Figure 2.2 : The continuous ozonation system with the necessary equipments: a peristaltic pump, a glass reactor with diffusers, a contact tank and an equalization tank.

A cylindrical glass reactor with a 2,200 mL effective volume was used which was fed with municipal wastewater via a peristaltic pump. The reactor had an outlet which allowed the wastewater to overflow to the contact tank. The reactor had an inlet from the top which allowed it to feed O₃ gas to the 4 ceramic diffusers located at the bottom

of the reactor. A peristaltic pump (Masterflex Easy-load 3 (Model 77800-62)) which had a flow rate range of 0.02 – 0.667 L/min was used to pump the wastewater to the reactor, where the flow rate of the system was ranged from 0.035 to 0.07 L/min. The flow rate of the continuous O₃-system was monitored to assure a constant flow rate. A contact tank (0.5 L) was used to achieve the desired contact time for the reaction of O₃. The water was then transferred to a 1 L equalization tank (glass beaker) via overflow using neoprene tubing. The equalization tank had an outlet to the drainage system in order to discharge the excess water.

The pumping rate required for the desired ozone dosage was calculated below for 4 mg/L as an example (Eq (2.1)).

Desired O₃ dosage: 4 mg/L

Minimum achieved O₃ production: 0.2 mg/min

$$\text{Pumping rate (Q)} = \frac{\text{Min O}_3 \text{ production}}{\text{Desired O}_3 \text{ dosage}} \quad (2.1)$$

$$\text{Pumping rate (Q)} = \frac{0.29 \text{ mg/min}}{4 \text{ mg/L}} \times \frac{60 \text{ min}}{1 \text{ hr}}$$

$$Q = 4.35 \text{ L/hr}$$

This flowrate was achieved by 20 rpm in the peristaltic pump.

$$Q_{\text{daily}} = 104.4 \text{ L/day (104 L is needed per day)}$$

Note that this volume was required daily and was collected from the WWTP. This volume is the highest volume that was required during the whole experimental plan. For 8 mg/L and 12 mg/L ozone dosage, the daily required volume was 70 L and 52 L, respectively.

Required volume of contact tank was calculated below for 4 mg/L ozone dosage as an example (Eq (2.2)). The required contact tank volume for the 4 mg/L dosage had the highest volume.

$$V_{\text{contact}} = Q_{\text{contact}} \times t_{\text{contact}} \quad (2.2)$$

$$V_{\text{contact}} = \frac{4.35 \text{ L}}{\text{hr}} \times \frac{1 \text{ hr}}{60 \text{ min}} \times 15 \text{ min}$$

$$V_{\text{contact}} = 1.1 \text{ L (for 4 mg/L O}_3 \text{ dosage)}$$

2.1.2 GAC/AIX/biochar column system

The filter columns had an inner diameter of 3.6 cm and a height of 15 cm with approximately 100 mL volume. Furthermore, the columns had a two layer plastic supporting material in both top and bottom in order to both avoid material leakage and to have a homogeneous flow. The supporting materials were suitable for the nominal diameters of all GAC, AIX and biochar materials. All the tubings in the system were 7 mm diameter plastic tubings with 4 mm inner diameter. A peristaltic pump (Ismatec, IPC Standard-Speed Digital Peristaltic Pump with Click-'N-Go Cartridges) with 12 channels was used to maintain the same drift in the pumps over time (Figure 2.3). The diameter of the peristaltic pump tubing was 1.42 mm for the GAC and biochar columns and 2.79 mm for the AIX and reference columns. The wall effect was neglected since it was smaller than 10% according to the calculations made based on Ozturk et al. (2020).



Figure 2.3 : The continuous GAC/AIX system with the necessary equipment: a multichannel peristaltic pump and plastic columns with necessary tubings.

The GAC was obtained from Chemviron (Cyclecarb 401) with a particle size range and surface area of 0.43-2.36 mm and 900 m²/g, respectively. The AIX was purchased

from Purolite (Purolite 694E) with a particle size of 0.68 ± 0.075 mm. The biochar 1 was derived from forest biomass, while biochar 2 was derived from undigested primary sewage sludge, where the sludge was collected from a WWTP of a small village ($\sim 7,000$ inhabitants). Similarly, the wall effect was neglected based on the calculations (Ozturk et al., 2020).

The GAC, AIX and biochar filter columns were operated in up-flow mode. The GAC and biochar empty bed contact time (EBCT) were 20 min, whereas the EBCT for AIX was 2 min. The filter columns were operated continuously for two weeks for each O_3 dosage. The filter material was changed at the end of each operational period. The empty bed volume (EBV) of the GAC/biochar columns and the AIX column were 30 cm^3 and 11.5 cm^3 , respectively. The flow rates of GAC/biochar columns and the AIX columns were 0.09 L/hr and 0.34 L/hr, respectively. The calculations for the flowrates were made according to Eq (2.3). The number of treated bed volumes was calculated by dividing the treated wastewater volume by the EBV of each column. At the end of 2 weeks operation, 864 BVs and 3,264 BVs for the GAC/biochar columns and AIX column were treated, respectively.

The designated flowrate to the each column was 0.09 L/hr.

Bed volume: $\pi D^2 h / 4 = \pi (3.6 \text{ cm})^2 3 \text{ cm} / 4 = 30 \text{ cm}^3 = 30 \text{ mL}$

$$Q_{\text{GAC/Biochar/AIX}} = \frac{V_{\text{bed}}}{t} \quad (2.3)$$

$$Q_{\text{GAC/Biochar}} = \frac{30 \text{ mL}}{20 \text{ min}} \times \frac{60 \text{ min}}{1 \text{ hr}} \times \frac{1 \text{ L}}{1000 \text{ mL}} = 0.09 \text{ L/hr}$$

$$Q_{\text{AIX}} = \frac{11.5 \text{ mL}}{2 \text{ min}} \times \frac{60 \text{ min}}{1 \text{ hr}} \times \frac{1 \text{ L}}{1000 \text{ mL}} = 0.34 \text{ L/hr}$$

The total required wastewater volume for 1 GAC, 2 biochar, 1 AIX and 1 reference column was approximately 0.96 L/hr. This value is important since the ozonation system had to produce at least this amount of water per hour. According to the calculations in section 4.1, the volume that was produced from the ozonation system was between 2 - 4 L/hr for different operation modes, which was enough for feeding all the columns.

Since the same multichannel peristaltic pump was used for GAC and AIX systems, where GAC has 1.42 mm diameter tubing and AIX has 2.79 mm tubing in the pump

channel, both systems was operated at the same rpm. This rpm (120 rpm) corresponds to the bed heights for GAC and AIX which was calculated above.

Table 2.1 : Experimental design calculations of the combined systems.

OZONE			GAC/Biochar/AIX COLUMNS		
Reactor			Diameter	3.6	cm
Min O ₃ dosage	0.29	mg/min	Height	15	cm
Desired O ₃ dosage	4	mg/L	V _{column}	152.6	mL
Pumping rate (Q)	4.35	L/hr			
Q _{daily}	104.4	L/day			
Max desired dose	15	mg/L	Peristaltic pump		
Min pumping rate	40	L/hr	GAC tubing diameter	1.42	mm
Peristaltic pump			Speed	120	%
Speed	0.072	rpm	Flowrate	2.15	mL/min
Q _{pump}	0.072	L/min	Q _{GAC}	0.13	L/hr
	5		AIX tubing diameter		mm
Q _{pumpneeded}	40	L/min		2.79	
New speed	20	rpm	Speed	120	%
Contact tank			Flowrate	8.2	mL/min
Contact time	15	min	Q _{AIX}	0.49	L/hr
V _{contact}	1.087	L	Common rpm	84	%
	5		Q _{GAC}		L/hr
Equalization tank				0.09	
V _{eq}	1	L	Q _{AIX}	0.34	L/hr
			Q _{totalreq}	0.96	L/hr
			Q _{daily}	4.35	L/hr
			Q _{dailymin}	1.42	L/hr
			GAC/Biochar columns		
			Contact time	20	min
			V _{bed}	30.10	cm ³
			Bed height	2.96	cm
			h _{bed}	3	cm
			AIX columns		
			Contact time	2	min
			V _{bed}	11.48	cm ³
			Bed height	1.13	cm
			h _{bed}	1	cm

2.2 Investigated Pharmaceuticals

In this study, 24 selected pharmaceuticals and 7 metabolites which include several oxidation transformation products were selected in order to monitor the system performance. The selected pharmaceuticals are based on previous studies, where all of them were detected in the Swedish wastewater (Golovko et al., 2021). The metabolites that were selected were based on various reasons. For instance, citalopram N-oxide that has been previously identified as a human metabolite and was also selected because it also is an ozonation transformation product (Hörsing et al., 2012). Similarly, 4 hydroxy diclofenac is the main active oxidative metabolite of diclofenac, where it is

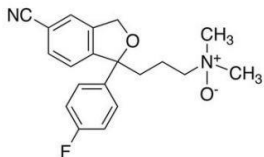
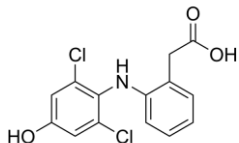
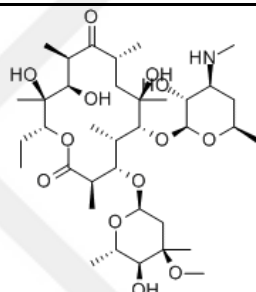
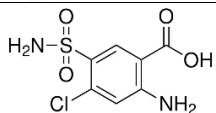
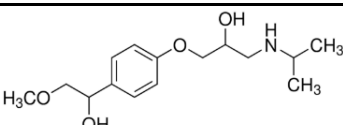
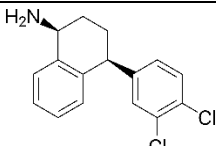
expected to be a transformation product of ozonation. On the other hand, compounds such as N-desmethylethromycin, 4-chloro-5-sulfamoylanthranilic acid (saluamine) and alpha-hydroxymetoprolol are the main metabolites of their parent compounds. Similarly, fluconazole N-oxide is one of the main metabolites of its parent compound, where norsesertraline (desmethyl sertraline) is an active metabolite of sertraline. All selected metabolites might be already in the inlet wastewater since they are metabolites of the human-body related physicochemical or biological processes, whereas some of them might be formed during the treatment processes such as oxidation by ozonation. It should be noted that desvenlafaxine is the major active metabolite of venlafaxine, whereas it has also been marketed separately as a serotonin-norepinephrine reuptake inhibitor (NLM, 2024). The properties of selected pharmaceuticals along with their metabolites are given in Table 2.2 and

Table 2.3. Among these metabolites, citalopram N-oxide and 4 hydroxy diclofenac are oxidation transformation products of their parent compounds. In total, 11 mass-labelled internal standards (IS) were used for quantification.

Table 2.2 : Properties including molecular weight (M_w) and octanol/water partition coefficient (K_{ow}) of the selected pharmaceuticals. NA = not available (*Source: National library of medicine (<https://pubchem.ncbi.nlm.nih.gov>)*).

Pharmaceutical	Class	Function	M_w	$\log K_{ow}$
Atenolol (ATN)	Beta-blockers	Inhibition of adrenalin and noradrenalin	266.3	0.16
Bicalutamide (MCL)	Antiandrogens	Blockage of testosterone	430.4	2.92
Carbamazepine (CRB)	Anticonvulsant	Psychiatric support	236.3	13.9
Cetirizine (CTR)	Antihistamine	Relief of allergic symptoms	388.9	1.70
Citalopram (CTL)	Antidepressant	Treatment of depression	324.4	1.39
Clarithromycin (CLR)	Antibiotic	Bacteria inactivation	747.9	3.16
Clindamycin (CLN)	Antibiotic	Bacteria inactivation	424.9	NA
Diclofenac (DCL)	NSAID	Inflammation reduction and pain relief	296.1	4.5
Desvenlafaxine (DSV)	Antidepressant	Treatment of depression	399.5	0.33
Erythromycin (ERY)	Antibiotic	Bacteria inactivation	733.9	3.06
Fexofenadine (FXF)	Antihistamine	Relief of allergic symptoms	501.7	0.3
Fluconazole (FLC)	Antifungal	Treatment of fungal infections	306.3	0.25
Furosemide (FRS)	Lipid regulator	Regulation of triglycerides	330.7	1.51
Irbesartan (IRB)	Cardiovascular agent	High blood pressure treatment	428.5	1.13
Lamotrigine (LMT)	Antiseizure	Epilepsy treatment	256.1	2.57
Losartan (LSR)	Cardiovascular agent	High blood pressure treatment	422.9	4.01
Metoprolol (MTP)	Cardiovascular agent	High blood pressure treatment	267.4	1.88
Oxazepam (OXZ)	Antidepressant	Treatment of depression	286.7	2.92
Propranolol (PRP)	Beta-blockers	Inhibition of adrenalin and noradrenalin	259.3	3.48
Sertraline (SRT)	Antidepressants	Treatment of depression	306.2	5.29
Sulfamethoxazole (SLF)	Antibiotic	Bacteria inactivation	253.3	0.89
Tramadol (TRD)	Analgesic	Pain relief	263.4	3.01
Trimethoprim (TRM)	Antibiotic	Bacteria inactivation	290.3	0.91
Venlafaxine (VNL)	Antidepressants	Treatment of depression	277.4	3.20

Table 2.3 : Selected metabolites of the pharmaceuticals with their properties including molecular weight (M_w) and chemical structure (*Source: National library of medicine (<https://pubchem.ncbi.nlm.nih.gov>)*)

Metabolite	Parent compound	M_w	Chemical structure
Citalopram N-oxide (CNO)	Citalopram	376.9	
4 hydroxy diclofenac (HDC)	Diclofenac	312. 2	
N-desmethylerythromycin (NDS)	Erythromycin	719.9	
Fluconazole N-oxide (FNO)	Fluconazole	322.3	
4-chloro-5-sulfamoylanthranilic acid (CSA)	Furosemide	250.7	
Alpha-hydroxymetoprolol (AHM)	Metoprolol	283.4	
Norsertraline (NRS)	Sertraline	292.2	

2.3 Characterization of the Feed Wastewater

The wastewater used for the laboratory-scale ozonation combined GAC/AIX/biochar system was collected from the effluent of Kungsängsverket WWTP, Uppsala, Sweden (Figure 2.4). The effluent was filtered at the WWTP by a pilot-scale sand filtration unit before sampling. Sand filtration is the already determined future pre-treatment for the quaternary treatment at this WWTP. The experiments were carried out with non-spiked original filtered effluent wastewater. The wastewater was collected every two or three days to feed the laboratory-scale system. An average characterization of the wastewater used in the tests is provided in Table A.1 in Appendix.

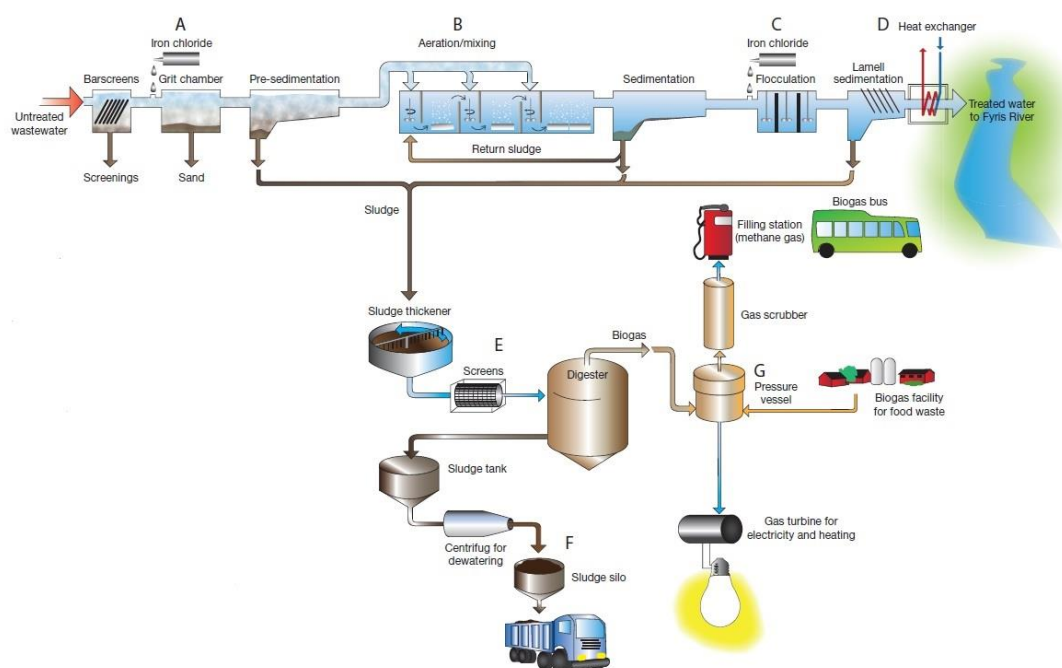


Figure 2.4 : Process configuration of the Kungsängsverket WWTP (Uppsala Water and Waste AB, 2019).

A study by Sörengård et al. (2019) revealed that the total OMP concentrations were reduced in the Kungsängsverket WWTP from 40,000 ng/L in the influent to 15,000 ng/L in the effluent, which corresponded to an average removal efficiency of 64% with respect to the individual OMP, although variation in removal efficiencies were greater. In the same study, results revealed that 25 out of 66 individual OMPs were removed in the WWTP to some extent, where these OMPs included the pharmaceuticals such as ibuprofen, naproxen, atenolol, clarithromycin, sertraline, furosemide, irbesartan, fluconazole, erythromycin, sulfamethozasole, diclofenac, trimetoprim, venlafaxine, oxazepam, metoprolol, fexofanadine.

2.4 Analytical and Instrumental Methods

2.4.1 Analysis of pharmaceuticals and transformation products

Analysis of the selected pharmaceuticals and their metabolites including transformation products were performed with SPE (solid phase extraction) followed by a DIONEX UltiMate 3000 ultra-high pressure liquid chromatography (UPLC) system (Thermo Scientific, Waltham, MA, USA) coupled to a triple quadrupole mass spectrometer (MS/MS) (TSQ QUANTIVA, Thermo SCIENTIFIC, Waltham, MA, USA). (Golovko et al., 2020). Native analytical standards were purchased from Sigma-Aldrich (Stockholm, Sweden). Isotopically labelled internal standards (ISs) were purchased from Teknolab AB (Kungsbacka, Sweden) and Toronto Research Chemicals (Toronto, ON, Canada). The data processing followed by the analysis was performed by TraceFinder 4.1 software (Thermo Fisher Scientific, USA) (...). The blank values were under the limit of quantification (LOQ) and the LOQ ranged from 2.6 to 220 ng/L (Table A.2 in Appendix A).

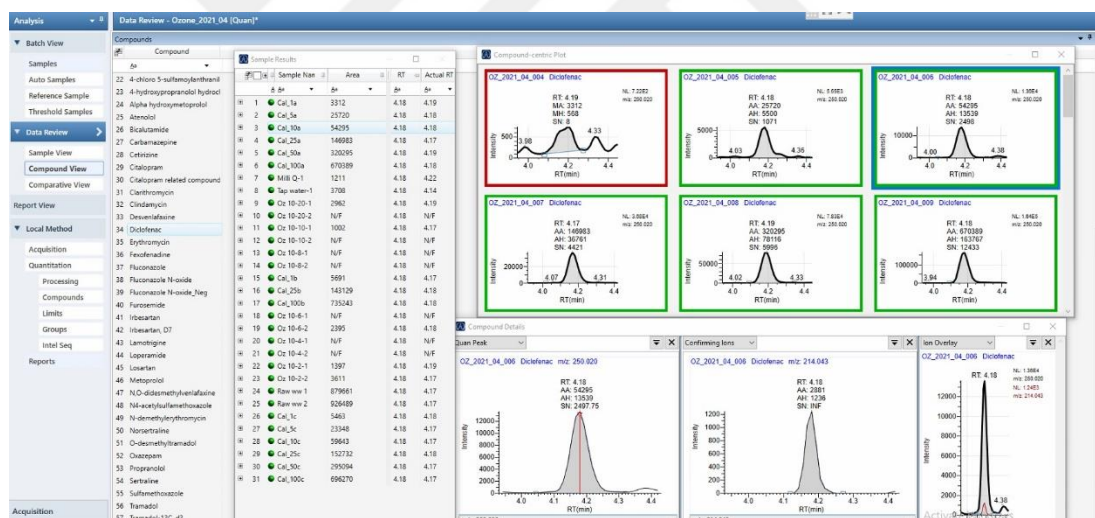


Figure 2.5 : Example of data review for the study by using TraceFinder.

Solid Phase Extraction (SPE) Steps were given below.

(1) Sample preparation: The sample bottles were thawed the day before filtering. For wastewater samples, 200 mL of sample volume is taken. For blanks, Milli-Q water and/or tap water was used and the blanks were filtrated first. Bottles were be cleaned with hot water and three times with EtOH before the experiment.

(2) Filtration: 250 mL clean plastic bottles were washed 2 times with EtOH. They were dried and labeled and the empty bottles were weighed. GF/F filters (catalog number

1825-047) were burned overnight in the oven at 400°C. The sample was shaken before filtration. The first 10mL of the sample was filtered, the system was cleaned and disregarded (This step is applied if only there is enough volume of the sample). Sample was filtered and the filtered sample was poured into the preweighed and labeled bottle, and then weighed again. The filtration unit and the beaker was cleaned before filtering samples from a new sampling site. They were cleaned with MQ water and EtOH.

Note: The filtration process was started by filtering the method blanks which is followed by field blanks and after that, the water or wastewater samples were filtered.

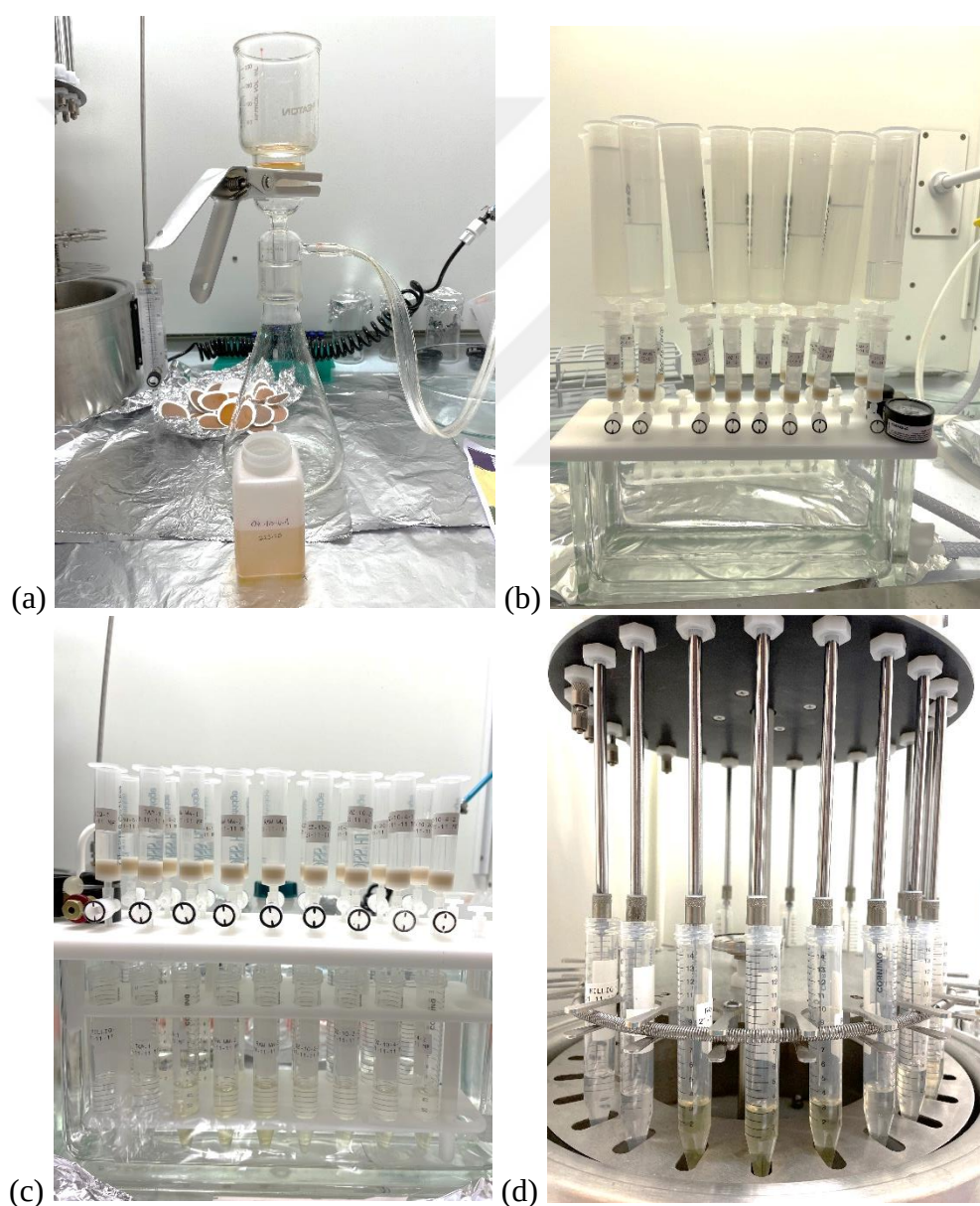


Figure 2.6 : SPE steps (a) Filtration (b) Extraction (c) Elution (d) Evaporation.

(3) Preparation before the extraction: 20 μ L (1 μ g/ml) of the internal standard mixture of the pharmaceuticals was added to each sample which was at room temperature. The mixture was spiked directly into the bottle and shaken.

(4) Preparation of extraction: Cartridges which are Oasis HLB (6cc, 200mg) were used. The SPE manifold, adapters, and stop-cocks were washed using EtOH two times and air dried. The white inner part of SPE station was removed prior to this cleaning step in order to keep it clean. The reservoirs were rinsed by dishwashing and EtOH. The SPE cartridges (Oasis HLB (200 mg, 6 mL)) were connected to the SPE manifold, adapter and reservoir and they were labeled.

(5) SPE extraction conditioning: 6 mL of methanol was added into each reservoir. 6 mL MQ water was added into each reservoir. The conditioning is done by gravity, without vacuum.

(6) SPE extraction: The samples were loaded onto SPE cartridges. In this step, water should flow at 1 drop/second using vacuum. The adapter and reservoir was removed. 6 mL MQ water was added directly into the cartridge. The cartridge was dried under vacuum for 20 min.

(7) SPE elution: The stop-cocks were rinsed with 2x MeOH with ultrasonication. The manifold lid was cleaned with EtOH and MilliQ. The SPE cartridges were connected to the SPE manifold and a clean plastic tube was placed under the outlet (it should be cleaned with EtOH). The plastic tube was labeled. 4 mL of methanol was added to the SPE cartridge and it was let drop by gravity (it was collected in the plastic tube). The vacuum was opened for 1 min. 4 mL of methanol was added to each SPE cartridge and it was let drop by gravity (it was also collect in the same plastic tube). The vacuum was opened for 1 min.

(8) Preparation of extract for HPLC: The samples were dried under nitrogen stream until approximately 0.5 mL. Each of the sample was then transferred to 1 mL an amber glass HPLC vial. The glass tubes were cleaned 3 times by adding methanol. The glass walls were rinsed with the same Pasteur pipette and transferred to the same HPLC vial. The samples were then evaporated to exact 0.5 mL. The extracts were vortexed for 30 seconds at speed 6. The extracts were kept in the freezer at -20°C until analysis. 0.5 mL MQ water was added to the extracts before HPLC analysis. The extracts were vortexed for 30 seconds and they were ready for LC-MSMS analysis.

2.4.2 Control of O₃ dosage

The actual O₃-dosage was regularly controlled via wet analysis by using an iodometric method. O₃-gas from the generator was exposed to 20 g/L potassium iodide (Supelco, USA) for 5 min before titration with 0.5 N Na₂S₂O₃ (Supelco, USA).

2.4.3 Conventional parameters and by-products

Measurement of pH, temperature, dissolved organic carbon (DOC), total organic carbon (TOC), alkalinity, total suspended solids (TSS), chemical oxygen demand (COD), nitrite nitrogen (NO₂-N), nitrate nitrogen (NO₃-N), ammonia nitrogen (NH₃-N), ultraviolet absorbance (UV₂₅₄), bromide (Br⁻) and bromate (BrO₃⁻) were carried out according to Water Quality Standards of International Organization for Standardization (ISO, 2019), Standard Methods (APHA, 2017) and Swedish Standards (SIS, 1996). Specific ultraviolet absorbance (SUVA₂₅₄) was calculated based on UV₂₅₄ and DOC. Since bromate is a carcinogenic oxidation by-product of bromide (Bourgin et al., 2018), both parameters were monitored throughout the whole study.

3. RESULTS AND DISCUSSION

3.1 Pharmaceuticals in the WWTP

In total, 23 of the 24 analyzed pharmaceuticals were found in the effluent wastewater obtained from the Kungsängsverket WWTP (Figure 3.1). According to the results, concentrations of sertraline, trimethoprim, fluconazole, atenolol and sulfamethoxazole were below 500 ng/L, whereas the concentrations of venlafaxine, desvenlafaxine, fexofenadine, bicalutamide and lamotrigine were above 5,000 ng/L on average. In total, 2 out of 5 pharmaceuticals that had the highest concentration were in the antidepressants class (venlafaxine and desvenlafaxine). The fluctuation (high standard deviation) in the pharmaceuticals' concentration might be related with the sampling period which was May to August, where some samples were diluted after rain. Among selected pharmaceuticals, nortriptyline was not detected in any analysis. The concentrations were generally in line with previous national Swedish screenings (Golovko et al., 2021; Fick et al., 2011; Malnes et al., 2022) and in the same range as in a previous studies in wastewater from the same WWTP (Beijer et al., 2017; Björlenius, 2018; Kalecinska, 2021) (Table 3.1).

According to the recent study by Hernández-Tenorio et al. (2022) conducted which includes 44 countries, the most frequently detected pharmaceuticals in the wastewater influents were sulfamethosazole, trimethoprim, ciprofloxacin, clarithromycin and erythromycin, acetaminophen, diclofenac, ibuprofen, naproxen and carbamazepine, where the aforementioned pharmaceuticals were also detected in the current study in the Swedish wastewater.

It should be noted that the concentrations of the pharmaceuticals in the wastewater greatly depends on the season, where as an example, the concentrations of the cold/flu related pharmaceuticals are expected to be greater in winter. Therefore, seasonal changes along with the other factors (such as dilution factor in the discharge point to

the receiving body) should be considered during the design of the quaternary treatment systems.

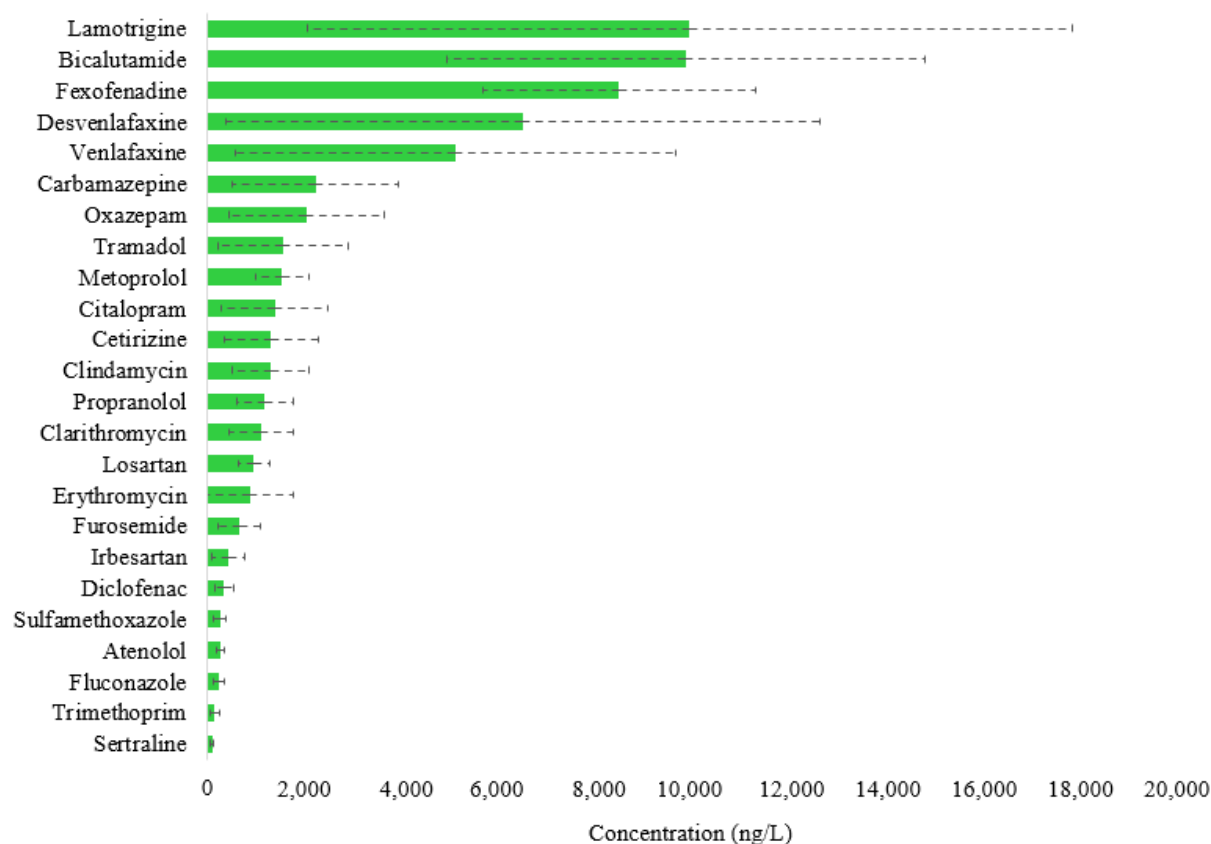


Figure 3.1 : Concentrations of pharmaceuticals in the effluent wastewater ($n = 10$) which was used for the laboratory-scale ozonation combined with GAC/AIX/biochar system experiments.

Table 3.1 : Average pharmaceutical concentrations in Kungsängsverket WWTP according to Beijer et al. (2017) and Björnlénus (2018).

Micropollutant	Björnlénus (2018)	Beijer et al. (2017)
Atenolol	220	154
Carbamazepine	524	304
Clarithromycin		21
Clindamycin		90
Citalopram	357	212
Diclofenac	200	210
Fexofenadine		149
Fluconazole		160
Irbesartan		54
Metoprolol	1095	1010
Oxazepam	330	257
Tramadol	563	437
Venlafaxine		363
Trimethoprim	77	61

3.2 Removal of Pharmaceuticals

3.2.1 Removal of pharmaceuticals via O₃-oxidation

Initially, 4, 8 and 12 mg/L O₃-dosages were selected for the three set of experiments, where the expected specific O₃-dosages were 0.4, 0.8 and 1.2 g O₃/g DOC as the average DOC concentration of the effluent wastewater was ~10 mg/L according to the previous measurements. However, during the sampling campaign, the DOC concentration of the wastewater from the WWTP has greatly varied. This led to higher specific O₃-dosages than desired for the two high O₃-dosages. According to the results presented in Figure 3.3 (for details see Table A.3 in Appendix A), average removal of selected pharmaceuticals ranged between 8.8 - 97% with an O₃-dose of 0.28 g O₃/g DOC, whereas it ranged from 86-99% for higher O₃-dosages (0.96 and 2.17 g O₃/g DOC). Compounds such as fluconazole, atenolol, metoprolol and tramadol had relatively lower removal rates (9-15%) with the specific O₃-dose of 0.28 g O₃/g DOC compared to furosemide, propranolol, clindamycin and clarithromycin with high removal rates (>90%).

Ozone tends to react with the electron donating (withdrawing) molecular groups such as —OH, —NH₂, while the possibility to react with the electron acceptors (—COOH, —NO₂, —Cl) such as itself is really low (von Sonntag and von Gunten, 2012). Tertiary amines such as cetirizine and fexofenadine which are known to have high reactivity with ozone had removal rates of 79% and 89% via 0.28 g O₃/g DOC in this study. Additionally, highly reactive compounds such as carbamazepine, diclofenac, sulfamethoxazole and trimethoprim were removed by 70%, 85%, 70% and 88% with 0.28 g O₃/g DOC. The results of the current study regarding the pharmaceutical removal via 0.28 g O₃/g DOC specific O₃-dosage were consistent with the literature (Edefell et al., 2021; Alameddine et al., 2021; Bourgin et al., 2018). In a study by Edefell et al. (2021), at the lowest dose of ozone, 0.3 g O₃/g DOC, ~20% of the 22 investigated OMPs were removed below the LOQ. In the abovementioned study, most of these completely removed compounds were highly reactive with ozone such as carbamazepine, diclofenac, sulfamethoxazole, and trimethoprim. Similarly, results of Alameddine et al. (2021) indicated that the high reactive compounds such as carbamazepine, sulfamethoxazole and naproxen were removed 80-100% with

ozonation of 0.27 g O₃/g DOC. Figure 3.2 depicts the comparison of the results from the current study with the literature for the 0.28 g O₃/g DOC ozone dosage (Edefel et al. 2021; Bourgin et al., 2018).

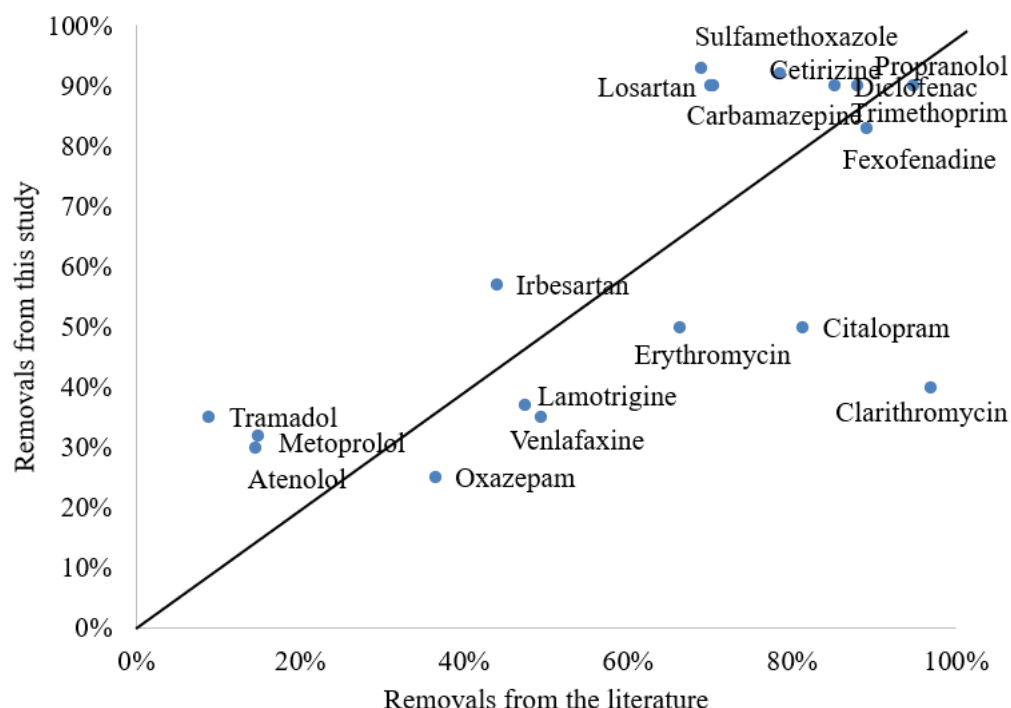


Figure 3.2 : Comparison of the results of the study with the literature for the 0.28 g O₃/g DOC ozone dosage.

According to Bourgin et al. (2018), substances with high reactivity with ozone at circumneutral pH such as diclofenac, carbamazepine, hydrochlorothiazide, sulfamethoxazole and tertiary amines such as cetirizine, fexofenadine and tramadol, were very well abated (>80%) even at 0.35 g O₃/g DOC. On the other hand, removal rates of erythromycin (66%), propranolol (94%), trimethoprim (86%), carbamazepine (71%), diclofenac (85%) and sulfamethoxazole (70%) in this study were lower than Guillossou et al. (2020)'s study with similar specific O₃-dosage. These differences may be attributed to varying wastewater qualities such as differing composition of the DOM leading to a lower ·OH formation (Schindler Wildhaber et al., 2015). Additionally, fluconazole had a removal rate of 9% with an O₃-dose of 0.28 g O₃/g DOC which was comparable with the literature (Alameddine et al., 2021; Östman et al., 2019). Similarly, atenolol was removed, on average, by 15% using 0.28 g O₃/g DOC in this study similar to Guillossou et al. (2020). For the higher O₃-dosages of 0.96 and 2.17 g O₃/g DOC, fluconazole was removed by 86% and 90%, respectively, in this study, which was much higher than the results presented by Alameddine et al.

(2021). In the study of Alameddine et al. (2021), pharmaceuticals such as fluconazole, which has intermediate-low interaction with ozonation, had removal rates of <50% with 2.17 g O₃/g DOC. Similarly, Östman et al. (2019) also found that ozone (0.55 g O₃/g TOC) was inefficient at removing benzotriazoles and fluconazole. In the current study, oxazepam was removed by 36% for the lowest dosage (0.28 g O₃/g DOC) which is higher than reported in the literature (Antoniou et al., 2013).

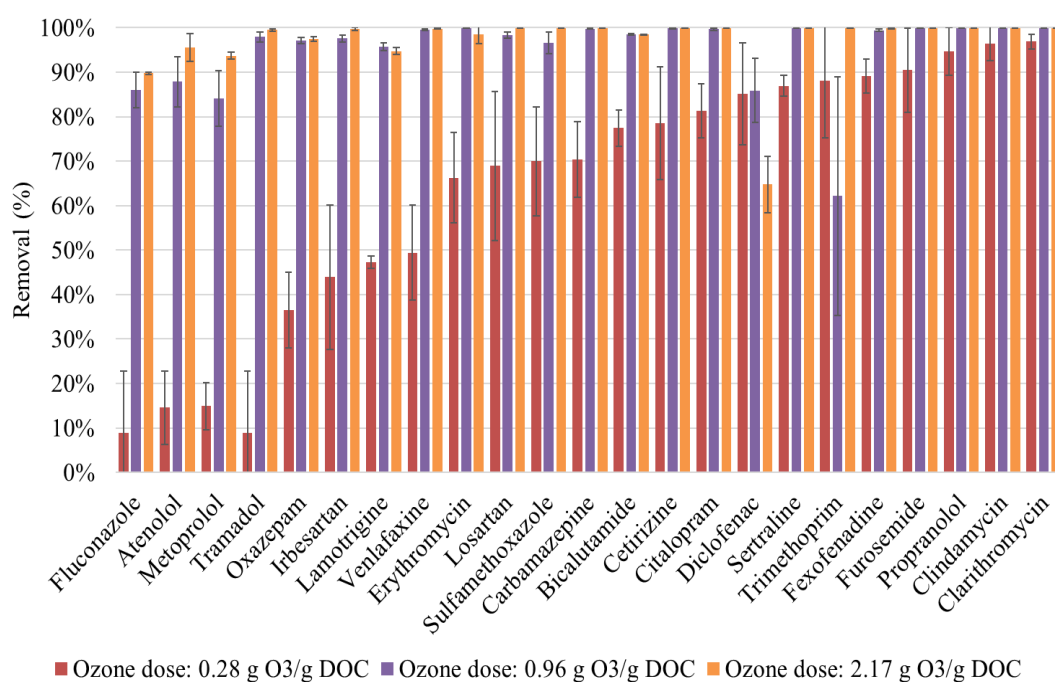


Figure 3.3 : Removal of pharmaceuticals via ozone at various O₃-dosages ($n = 3$).

The measured concentrations in the equalization tank and the reference column can be used as a measure of the stability of the experimental set-up, and the same or similar concentrations represent a stable system. Figure A.1 in the Appendix A represents the concentration difference between the equalization tank and the reference column in percentage in all samples that had results above LOQ ($n = 2-9$). In total, 19 out of 24 pharmaceuticals were measured within $\pm 20\%$ difference between the two aforementioned sampling points on average, and the difference amongst all pharmaceuticals was 8% on average. In conclusion, this variation was in the same range as the analytical uncertainty, which indicates that the system setup was verified by the reference column.

3.2.2 Removal of pharmaceuticals via sorption systems

GAC was the best performing sorbent among all materials, where even after two weeks of continuous operation (BV=864), nearly all compounds were removed below LOQ (Table 3.2). It should be noted that “>” means the compound has been removed beyond the LOQ. This is in accordance with the literature, for example, Guillosoou et al. (2019) studied pilot-scale GAC systems for the removal of 48 OMPs, which showed removal efficiencies of 20-99% for pharmaceuticals. A pilot scale study by Altmann et al. (2016) showed that well adsorbing OMPs (e.g. benzotriazole, carbamazepine) were removed by >80% at 8,000-10,000 BV, whereas weakly to medium adsorbing OMPs (e.g. primidone, sulfamethoxazole) showed removals <80% at <5,000 BV. Both carbamazepine and sulfamethoxazole removal was >99% in this study which were similar to the literature (Guillosoou et al., 2019; Altmann et al., 2016; Kalecinska et al., 2021). A similar study by Kalecinska (2021) with the same type of GAC (Cyclecarb-401) and using the same wastewater source revealed that the removal of the selected pharmaceuticals ranged between 87-100% after 48 h. In the aforementioned study; metoprolol, tramadol, clarithromycin and erythromycin were removed 100%, whereas atenolol, carbamazepine, citalopram and oxazepam were removed by 99%. In addition, furosemide, irbesartan and losartan were removed by 98%, fluconazole by 96%, sulfamethoxazole by 87% and sertraline by 39%. It can be concluded that the results of the removal of pharmaceuticals using GAC in this study was similar with the results of Kalecinska (2021)’s study.

Removal of selected pharmaceuticals by biochar 1 (derived from forest biomass) and biochar 2 (derived from sewage sludge) are presented in Table 3. Since biochar 2 was derived from the sewage sludge, the possible success of especially the biochar 2 for the removal of pharmaceuticals were quite important for the overall sustainability in the WWTP. Although biochar 1 showed a better performance than biochar 2, both sorption materials showed reduced sorption capacity over the time period of two weeks (BV=864) for most of the target compounds including carbamazepine, fexofenadine, tramadol, fluconazole, sulfamethoxazole and erythromycin. At the end of 2 weeks of continuous operation, biochar 1 showed removal rates between 30-89% (mean 68%), whereas removal by biochar 2 of the selected compounds were 8.5-82% (mean 38%). The highest removal rates with biochar 1 were obtained for metoprolol (89-99%), oxazepam (83-97%) and fexofenadine (82-98%), whereas the lowest removal rates

were obtained for carbamazepine (30-78%), clarithromycin (35%) and sertraline (47%) during the two weeks operation time. The performance of biochar 2 was poorer, where the removal rates of many compounds such as carbamazepine (18%), cetirizine (25%), clarithromycin (35%), tramadol (22%), fluconazole (9%), irbesartan (37%), losartan (32%), sulfamethoxazole (27%), erythromycin (29%) and venlafaxine (31%) dropped drastically at the end of 2 weeks compared to the 5th day sample. These results are comparable with the literature showing that the adsorption of metoprolol and carbamazepine was high with non-activated hard wood biochar (99% removal after 22 weeks for both compounds) (Dalahmeh et al., 2018).

On the other hand, AIX which has been included as it is used for PFAS removal (Kalecinska et al., 2021), had as expected lower removal rates after 2 weeks compared to biochars 1 and 2 ranging between 2-55% (average: 20%) for the positive removal rates (3,264 BV) (Table 3.2, Table A.1 in Appendix A). However, several compounds had slightly negative removal rates (e.g., sertraline, metoprolol, tramadol and fluconazole) ranging from -26 to -2%. It should be noted that since higher flowrates and higher material volume with the same diameter was used in the AIX columns, the risk of channel formation was very high compared to the other columns, which might have been resulted in much lower EBCT than assumed. Therefore, this might have negatively affected the results of AIX. The study of Kalecinska (2021) reported that the removal rates of the most pharmaceuticals were negative using AIX filters, whereby the pharmaceuticals such as atenolol, metoprolol, tramadol, carbamazepine, citalopram, fluconazole, oxazepam, clarithromycin, erythromycin and sertraline had negative removal ratios ranging from -83 to -4 % in the reference study. Therefore, the results from this study were in line with Kalecinska (2021)'s study. The negative results might be related with the type of AIX resin (PFA694E, Purolite), which is a polymer which has a structure of polystyrene cross-linked with divinylbenzene. This polymer is designed to remove PFAS and therefore, it might have functional groups that might adversely affect the removal of selected pharmaceuticals which might cause negative removal rates. In addition, experimental and analytical uncertainties can explain in some cases the slightly negative results. The highest removal rates in this study showed diclofenac (44-82%) which was followed by irbesartan (45-64%) and losartan (50-66%) throughout the whole operation duration of 2 weeks.

Table 3.2 : Removal of pharmaceuticals using a) GAC, b) AIX, c) biochar 1, and d) biochar 2. The water to the various columns had been treated with an O₃ dose of 0.28 g O₃/mg DOC and the removal rates represent the removal only based on the sorbent materials. “>” means that the process was successful at removing the compound below LOQ. NA means not available since the previous ozonation process had already removed the compound below LOQ.

Micropollutant/Day	GAC			AIX			Biochar 1			Biochar 2		
	1	5	12	1	5	12	1	5	12	1	5	12
Atenolol	>95%	>95%	>95%	2.0%	5.4%	4.6%	>95%	>95%	78%	79%	74%	71%
Metoprolol	>99%	>99%	>99%	-18%	-9.2%	-10%	>99%	99%	89%	87%	89%	73%
Carbamazepine	>97%	>94%	>94%	12%	1.9%	-2.4%	>97%	78%	30%	66%	25%	18%
Cetirizine	>94%	>86%	>79%	40%	44%	6.3%	>94%	>86%	66%	69%	54%	25%
Citalopram	>91%	>83%	>84%	-13%	-2.1%	-7.3%	>91%	>83%	84%	>91%	>83%	80%
Oxazepam	>98%	>99%	>98%	13%	26%	3.1%	>98%	97%	83%	73%	76%	51%
Lamotrigine	>98%	>99%	99%	-1.2%	8.2%	2.2%	99%	95%	67%	72%	71%	48%
Bicalutamide	>99%	>99%	>99%	41%	53%	40%	>99%	>99%	97%	96%	96%	82%
Clarithromycin	>37%	>28%	>35%	-39%	-14%	16%	>37%	>28%	35%	>37%	>28%	35%
Clindamycin	>86%	>53%	NA	-26%	1.6%	NA	>86%	>53%	NA	85%	>53%	NA
Fexofenadine	>99%	>99%	>99%	-12%	8.5%	3.0%	>99%	98%	82%	81%	71%	47%
Propranolol	>90%	>65%	NA	-24%	-26%	NA	>90%	>65%	NA	>90%	>65%	NA
Tramadol	>99%	>98%	>97%	-15%	26%	-23%	>99%	92%	61%	63%	52%	22%
Fluconazole	>96%	>97%	>95%	-6.5%	24%	-13%	>96%	92%	58%	60%	52%	8.5%
Diclofenac	>98%	>95%	>79%	56%	82%	44%	>98%	91%	50%	72%	49%	-39%
Furosemide	>89%	>49%	NA	61%	42%	NA	>89%	>50%	NA	57%	>49%	NA
Irbesartan	>86%	>87%	>80%	54%	64%	45%	>86%	>87%	73%	68%	64%	37%
Losartan	>96%	>96%	>85%	50%	66%	55%	>96%	95%	70%	72%	67%	32%
Sulfamethoxazole	>87%	>87%	>70%	15%	49%	33%	>87%	86%	63%	39%	44%	27%
Trimethoprim	>79%	>18%	NA	-15%	-19%	NA	>79%	>18%	NA	>79%	>18%	NA
Erythromycin	>99%	>98%	>98%	-6.2%	-6.8%	3.2%	>99%	91%	63%	57%	30%	29%
Sertraline	>58%	>47%	>46%	2.9%	47%	-26%	>58%	47%	46%	>58%	47%	46%
Venlafaxine	>99%	>99%	>98%	-15%	-1.5%	-3.5%	>99%	93%	70%	64%	52%	31%
Desvenlafaxine	>98%	>97%	>98%	-15%	2.4%	1.0%	>98%	92%	71%	69%	52%	47% ^s

NA=not available

3.2.3 Performance of combined system using ozonation and sorbent filters for pharmaceuticals

Since the higher O_3 -dosages (0.96 and 2.17 g O_3 /g DOC) removed most of the selected pharmaceuticals below or close to the LOQ, the evaluation of the combined systems was performed using the lowest O_3 -dosage of 0.28 g O_3 /g DOC in order to observe the effect of both processes in the hybrid systems. Figure 3.4 depicts the removal rates of pharmaceuticals via combined systems on the 5th day of operation, where it was considered to be the most representative sampling point in terms of comparison. According to the results, GAC showed the best performance in combination with ozone (>99%), followed by biochar 1. For instance, tramadol was removed by 8.8% with 0.28 g O_3 /g DOC, then the rest of the compound was removed by GAC (>91%), whereas the portion that was left after ozonation were removed separately by biochar 1, biochar 2 and AIX were 84%, 42% and 23%, respectively. Another compound, carbamazepine, was removed by 70% via ozonation, whereas it was removed by GAC, biochar 1, biochar 2 and AIX by >30%, 23%, 7.3% and 0.6%, respectively. Overall, the combination of ozone with biochar 1 was more successful (mean=91%, 42-99%) than the combination with biochar 2 (mean=79%, 29-99%). The combination of ozone with AIX showed as expected the lowest removal rates for pharmaceuticals (mean=58%, 6-98%). However, since the PFAS removal by O_3 -AIX combination was aimed to be studied in the future by the aforementioned WWTP, results obtained from this study in terms of pharmaceuticals removal were utmost important as a base study.

Results of the study in terms of ozone combination with GAC complied with the literature. For instance, Östman et al. (2019) presented the effect of full-scale ozonation and pilot-scale GAC on the removal of biocides, antimycotics and antibiotics in a WWTP. O_3 (0.55 g O_3 /g TOC) was not effective to remove the benzotriazoles and fluconazole, whereas high removal efficiency (>99%) of several compounds were obtained by utilizing GAC filtration after ozonation. Similarly, Vatankhah et al. (2019) found that the removal of a wide range of OMPs including pharmaceuticals was improved using O_3 -GAC treatment trials when compared to the combined removal observed in separate ozonation and GAC adsorption experiments. Since there is very limited O_3 -biochar and O_3 -AIX study in the continuous systems in the literature, relevant comparison could not be effectively performed.

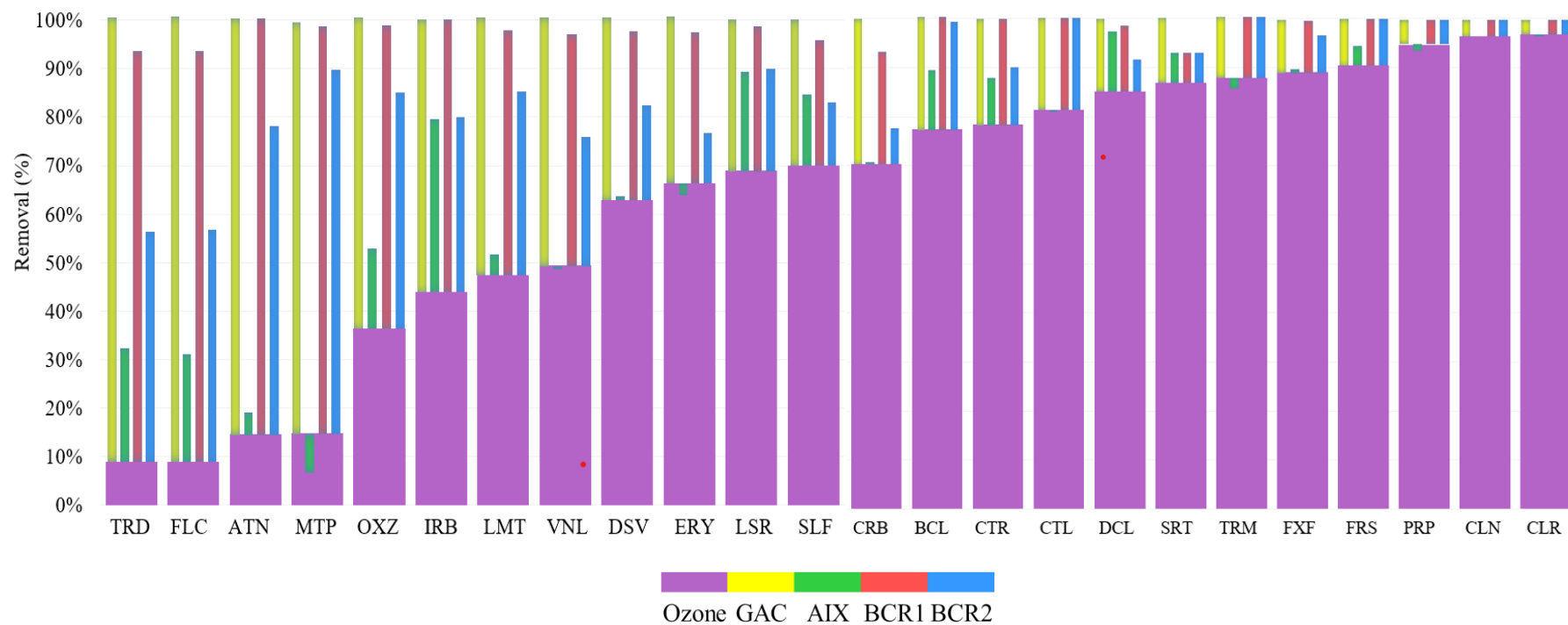


Figure 3.4 : Overall removal rates of selected pharmaceuticals (for abbreviations see Table 1) via O₃-oxidation using 0.28 g O₃/mg DOC followed by sorption systems using a) GAC, b) AIX, c) biochar 1 and d) biochar 2 after 7 days of continuous operation. Please find the abbreviations of the pharmaceuticals in Table 2.2).

3.3 Fate of Metabolites and Oxidation Transformation Products

3.3.1 Fate of transformation products after ozonation

According to the results, 6 out of 7 metabolites were detected in samples both before and after ozonation (Table A.4 in Appendix A). Among 7 metabolites, alpha hydroxymetoprolol, citalopram related compound E, fluconazole N-oxide, 4 hydroxy diclofenac, 4-chloro 5-sulfamoylanthranilic acid and desvenlafaxine were detected in the filtered effluent of the WWTP, whereas N-demethylerythromycin was not detected in any samples. 4 hydroxy diclofenac was not detected after all columns after the 1st, 5th and 12th day. Results indicated that the concentrations of some metabolites decreased during ozonation, whereas the concentration of some metabolites that also are known oxidation transformation products (such as citalopram N-oxide) increased during the two weeks of continuous operation. Figure 3.5 depicts increase of citalopram N-oxide (citalopram related compound E) and the parent compound citalopram throughout different O₃-dosages. Citalopram concentration was decreased by 81% on average, while citalopram related compound E concentration was increased by 19% with the O₃ dosage of 0.28 g O₃/ g DOC. When the system was operated with 2.17 g O₃/ g DOC, the average removal of citalopram reached to LOQ, while the increase in citalopram related compound E was above 33%. On the other hand, since the alpha hydroxymetoprolol is formed by the hydroxylation of the aliphatic side chain of metoprolol, it is not expected to be increased after the ozonation. Therefore, it has been eliminated via oxidation along with its parent compound. Overall, the metabolites exhibited lower reactivity with ozone compared to the parent compounds, similar to Kharel et al. (2021).

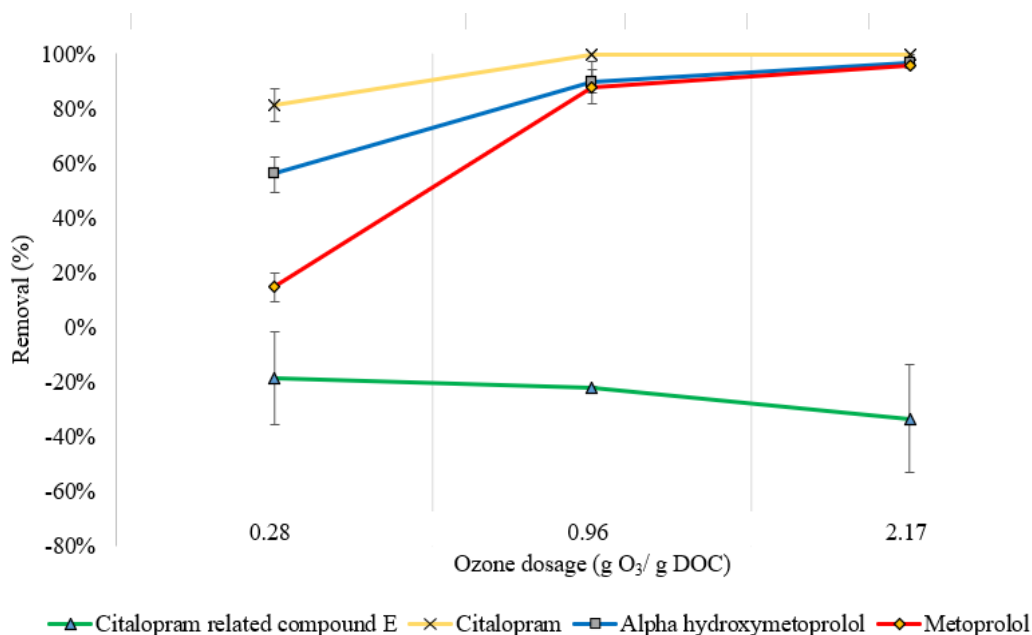


Figure 3.5 : Fate of citalopram and metoprolol with their metabolites at different O₃ dosages throughout the two weeks operation period.

Fluconazole N-oxide was removed between 78-99% (88% on average) for all O₃-dosages. Similarly, desvenlafaxine was removed by 94-99% in all O₃-dosages. Since the 4 hydroxy diclofenac is an oxidative metabolite of diclofenac, it was expected to be formed during ozonation. However, the concentration of 4 hydroxy diclofenac was found to be quite low in the inlet wastewater (4.6 ng/L), where it was decreased until the LOQ (<2.6 ng/L) after the ozonation. This result might be explained by the occurrence of the catalytic reaction during ozonation. 4-chloro 5-sulfamoylanthranilic acid was removed by 48% in the lowest O₃-dosage (0.28 g O₃/g DOC) while it was removed until the LOQ in the highest dosage of ozone (2.17 g O₃/g DOC). Finally, N-demethylerythromycin was not detected prior to or after ozonation in all cases. Overall, since the LOQs for transformation products were rather high, which might be the main reason why some compounds were not detected in the samples.

3.3.2 Fate of transformation products after GAC, AIX and biochar filters

Fate of the metabolites, which includes several oxidation transformation products, throughout the columns were evaluated via the first operation time that was after the lowest O₃-dosage, where the removal by the columns could be seen more clearly. Results indicated that all detected metabolites were eliminated until LOQ using GAC after 2 weeks of operation. Alpha hydroxymetoprolol removal was increased in time

using AIX, where the removal was 0.6%, 6.6% and 12% at the 1st, 5th and 12th day of operation. Removal of alpha hydroxymetoprolol via biochar 1 was decreased from 91% to 78% from day 1 to day 14. Similarly, the removal of alpha hydroxymetoprolol via biochar 2 was 77%, 71% and 55% at the 1st, 5th and 12th day of operation, respectively, showing a linear decrease in time. Removal of citalopram related compound E, which is an ozonation transformation product, with AIX was between 5.0-25% during the operation, whereas it was 66-80% and 55-80% for biochar 1 and biochar 2 with a decrease in removal with time. 4-chloro 5-sulfamoylanthranilic acid was removed 7.6-28% with AIX throughout 2 weeks of operation, whereas the removal of the compound via biochar 1 was gradually decreased in time on the 1st (99.9%) 5th (56%) and 12th (22%) day. Similarly, biochar 2 removal efficiency decreased over time for 4-chloro 5-sulfamoylanthranilic acid, but overall the removals (12-52%) were lower than biochar 2. Last but not least, desvenlafaxine removal via AIX was 13-35%. Biochar 1 removed the desvenlafaxine by 96.9% on the first day, 52% on the 5th day and 14% on the 12th day, while biochar 2 efficiency ranged between 0-70% for the compound. Compounds such as 4 hydroxy diclofenac, N-demethylerythromycin and fluconazole N-oxide were not detected in the effluent of all columns due to the elimination via previous ozonation process. It should be noted that for some metabolites, the LOQ was higher than for their parent pharmaceuticals, which might be the cause of not detecting the compounds in several samples.

3.4 Monitoring of Other Parameters

The bromate concentrations during all three O₃-dosages (0.28, 0.96 and 2.17 g O₃/g DOC) were below 5 µg/L. At the lower O₃-dosage of 0.28 O₃/g DOC, the bromide concentration in the used WWTP-effluent was 1.03 mg/L, whereas at the higher O₃-dosages of 0.96 and 2.17 g O₃/g DOC, the bromide concentrations were 0.52 and <0.50 mg/L, respectively. This fluctuation has resulted in inability to evaluate the potential formation of bromate. Since actual wastewater was utilized in the experiments, the change in bromide concentrations were not controllable. The bromide levels were constant through all column lines for the first operation period (0.28 O₃/g DOC), where it was measured as 1.05, 1.04, 1.07, 1.07 and 1.08 mg/L for GAC, AIX, reference column, biochar 1 and biochar 2, respectively. Similarly, in the second operation period (0.96 O₃/g DOC), the bromide levels for GAC, AIX, reference column, biochar

1 and biochar 2 were 0.56, 0.59, 0.58, 0.57 and 0.59 mg/L, respectively. Finally, in the last operation period, bromide concentrations in all columns were below 0.50 mg/L.

Removal of DOC via different O₃-dosages (0.28, 0.96 and 2.17 g O₃/g DOC) were 19-26%, while the removal of DOC via GAC was above 90% during all operational conditions. On the other hand, AIX only removed less than 10% of initial DOC during all operational conditions. Biochar 1 removed 18-23% of the initial DOC, whereas biochar 2 only removed 5-10% in all cases. Therefore, GAC was the most successful sorption material among all materials tested in the study in terms of DOC removal.



4. CONCLUSIONS AND RECOMMENDATIONS

Ozonation is one of the most extensively studied oxidative processes for the removal of pharmaceuticals from wastewater. However, the key findings from the literature review regarding the sole ozonation systems in terms of abatement of pharmaceuticals from the biological wastewater treatment plant effluents are as follows: (1) Achieving better efficiency through an ozonation system based on the wastewater characteristics is highly dependent on the operational and design parameters such as ozone dosage, HRT and dispersion method. (2) The impact of the treatment system scale on the removal of pharmaceuticals in the wastewater via ozone should be considered while comparing similar studies. (3) Although there is often mechanistic information available for the ozonation transformation products, there are still significant knowledge gaps on degradation pathways which should be the focus of future studies. (4) To eliminate the challenges that are imposed by by-products of ozonation, a biological or physical post-treatment step is recommended to reduce the undesirable impacts on the receiving water bodies.

More attention should be paid to the following issues in terms of sole GAC, AIX and biochar systems: (1) The removal of OMPs greatly depends on the operation time of the GAC system, where the breakthrough for each compound depends on their physicochemical properties and the quality of the wastewater. (2) Most pharmaceuticals are weak organic acids or bases, which makes their sorption onto oppositely charged polymers such as AIX even stronger than onto activated carbon. Additionally, other molecular level bonds also contribute to the removal process such as Coulombic interactions, van der Waals and H-bonding. (3) Biochar has great potential as an alternative adsorbent to activated carbon since it is a more sustainable material and it has superior physicochemical characteristics such as high specific surface areas, large pore volumes, and abundant functional groups. (4) The effectiveness of the biochar in terms of the removal of OMPs was found to have a strong connection with factors such as the aromaticity index, polarity index, specific

surface area and the presence of oxygen functional groups. (5) Conducting bench-scale continuous flow experiments is necessary to gain a more comprehensive understanding of the practical utility of biochar. Moreover, further research is essential to evaluate the effectiveness of biochar in real wastewater treatment scenarios, taking into account natural environmental conditions and the presence of other pollutants.

Ozone oxidation combined with activated carbon adsorption is a hybrid system that is considered as widely used to increase the removal efficiency of pharmaceuticals from wastewater by eliminating the limitations of each single treatment which results in the treatment train becoming more efficient. Important aspects to be considered in terms of the combination of ozone with activated carbon system are as follows: (1) The combination of these two technologies enables the limitations of each single treatment to be reduced and allows the treatment train to become more efficient. Adsorption via GAC can not only remove unoxidized pollutants but also the human carcinogenic byproducts of ozonation. (2) The removal efficiencies of the pharmaceuticals greatly depend on the wastewater characteristics such as DOM, where competition between the DOM and the pharmaceuticals is expected to occur in the oxidation and adsorption processes. (2) Ozonation can both remove the adsorption-refractory compounds and oxidize DOM where it can reduce the competition of DOM with pharmaceuticals and their transformation products onto activated carbon, which results in limiting the decrease of activated carbon adsorption capacity over time. (4) Ozonation alters the larger DOM molecules into smaller ones with decreased aromaticity and hydrophobicity, leading to a decrease in their adsorption capacity. This reduced adsorption reduces their interference with OMP adsorption, ultimately enhancing the removal of OMPs.

4.1 Conclusions of the Study

Ozonation showed high removal efficiency of pharmaceuticals and their metabolites at higher O_3 -dosage ($>0.96 O_3/g$ DOC), whereas at lower O_3 -dosage ($0.28 g O_3/g$ DOC), a post-treatment was necessary for efficient removal of pharmaceuticals. However, high O_3 -dosages increase operational costs and the risk of formation of transformation products. Therefore, utilizing combined systems for the elimination of pharmaceuticals and their metabolites is suggested as a better option compared with ozonation as the only advanced treatment system. The comparison of different post-

treatment filter sorbents showed the best results for removal of pharmaceuticals and their metabolites using GAC. On the other hand, the adsorption capacities of two different types of biochars decreased over the two weeks of continuous operation, whereas GAC had the same throughout the operation time. Biochar 1 showed a better performance than biochar 2 in terms of pharmaceutical removal. Lowest removal efficiencies were observed for AIX resulted partly because of the lower applied contact time, which implies that AIX would not be sufficient as a polishing step for the ozonation when aiming for the simultaneous removal of pharmaceuticals and PFAS. Overall, the combination of O₃ with GAC showed the best performance for removal of pharmaceuticals.

4.2 Practical Application of This Study

Biochar has a potential for becoming an alternative to GAC as a more sustainable sorbent since it can be obtained from renewable materials such as wood. Further development is, however, required in order to better understand the efficiency of combined O₃-filter systems, long term operation of the combined systems should be considered. For scaling up to the full-scale WWTP, a life cycle assessment might be helpful before making further decisions, along with conducting a feasibility analysis.



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APPENDICES

APPENDIX A: Supplementary data



APPENDIX A : Supplementary data

Table A.1 : Characterization of the effluent wastewater used in the tests.

Parameter	Unit	Mean±standard deviation
pH	-	7.53±0.12
Temperature	°C	18.6±1.12
Dissolved organic carbon (DOC)	mg/L	9.42±3.70
Total organic carbon (TOC)	mg/L	9.98±4.12
Alkalinity	mg CaCO ₃ /L	166±38
Total suspended solids (TSS)	mg/L	11.8±8.25
Chemical oxygen demand (COD)	mg/L	28.2±11.2
Nitrite nitrogen (NO ₂ -N)	mg/L	0.01±0.01
Nitrate nitrogen (NO ₃ -N)	mg/L	8.21±3.02
Ammonia nitrogen (NH ₃ -N)	mg/L	0.11±0.13
UV ₂₅₄	cm ⁻¹	0.14±0.04
Bromide (Br ⁻)	mg/L	0.53±0.41
Bromate (BrO ₃ ⁻)	µg/L	<5.0
Specific ultraviolet absorbance (SUVA ₂₅₄)	mg/L.cm	1.60±0.21

Table A.2 : LOQ values of all selected pharmaceuticals and their metabolites.

Pharmaceutical	LOQ
Atenolol	< 7.2
Bicalutamide	< 8.6
Carbamazepine	< 5.4
Cetirizine	< 5.6
Citalopram	< 4.4
Clarithromycin	< 7.1
Clindamycin	< 7.7
Desvenlafaxine	< 5.1
Diclofenac	< 3.1
Erythromycin	< 12
Fexofenadine	< 8.7
Fluconazole	< 6.4
Furosemide	< 7.6
Irbesartan	< 7
Lamotrigine	< 5.5
Losartan	< 11
Metoprolol	< 7.1
Oxazepam	< 4.9
Propranolol	< 8.1
Sertraline	< 4.9
Sulfamethoxazole	< 11
Tramadol	< 6.5
Trimethoprim	< 11
Venlafaxine	< 4.2
Metabolite	LOQ
4 hydroxy diclofenac	< 2.6
4-chloro 5-sulfamoylanthranilic acid	< 75
Alpha hydroxymetoprolol	< 6.2
Citalopram related compound E	< 5.2
Fluconazole N-oxide	< 7.6
N-demethylerythromycin	< 11
Norsertraline	< 220

Table A.3 : Concentrations of the selected pharmaceuticals in the filtered effluent and after each treatment step.

Ozone dosage: 0.28 g O₃/ g DOC - Day 1							
Micropollutant	Filtered Effluent	Equalization Tank	GAC	AIX	Reference	Biochar 1	Biochar 2
Atenolol	175	147	< 7.2	146	149	< 7.2	31.9
Metoprolol	1773	1615	< 7.1	1637	1383	< 7.1	180
Carbamazepine	387	179	< 5.4	142	161	< 5.4	54.3
Cetirizine	240	114	< 5.6	56.4	94.1	< 5.6	29.6
Citalopram	179	58.8	< 4.4	55.1	48.7	< 4.4	< 4.4
Oxazepam	466	332	< 4.9	258	294	< 4.9	78.5
Lamotrigine	2005	1164	17.4	1068	1055	8.9	296
Bicalutamide	6517	2228	< 8.6	1085	1844	< 8.6	68.5
Clarithromycin	203	18.8	< 7.1	15.8	11.3	< 7.1	< 7.1
Clindamycin	630	74.5	< 7.7	70.5	56.0	< 7.7	8.2
Fexofenadine	8387	1868	< 8.7	1488	1332	< 8.7	255
Propranolol	638	118	< 8.1	100	81.2	< 8.1	< 8.1
Tramadol	502	593	< 6.5	519	450	< 6.5	166
Fluconazole	150	187	< 6.4	168	157	< 6.4	62.8
Diclofenac	540	198	< 3.1	71.8	163	< 3.1	44.9
Furosemide	302	69.5	< 7.6	26.2	67.6	< 7.6	29.3
Irbesartan	69	54.5	< 7	22.6	49.4	< 7	15.8
Losartan	558	344	< 11	144	288	< 11	80.5
Sulfamethoxazole	188	134	< 11	74.9	87.6	< 11	53.5
Trimethoprim	176	62.4	< 11	60.5	52.4	< 11	< 11
Erythromycin	2094	834	< 12	850	800	< 12	342
Norsertaline	< 220	< 220	< 220	< 220	< 220	< 220	< 220
Sertraline	76.8	19.4	< 4.9	11.2	11.5	< 4.9	< 4.9
Venlafaxine	482	392	< 4.2	344	299	< 4.2	108
Desvenlafaxine	544	359	< 5.1	329	287	< 5.1	88.2

Table A.3 (Continued): Concentrations of the selected pharmaceuticals in the filtered effluent and after each treatment step.

Ozone dosage: 0.28 g O₃/ g DOC - Day 5							
Micropollutant	Filtered Effluent	Equalization Tank	GAC	AIX	Reference	Biochar 1	Biochar 2
Atenolol	153	124	< 7.2	138	146	< 7.2	37.6
Metoprolol	1876	1330	< 7.1	1771	1622	16.0	186
Carbamazepine	378	76.0	< 5.4	84.1	85.7	19.1	64.5
Cetirizine	261	36.0	< 5.6	22.0	39.3	< 5.6	17.9
Citalopram	181	23.7	< 4.4	25.9	25.3	< 4.4	< 4.4
Oxazepam	461	304	< 4.9	254	342	9.1	82.8
Lamotrigine	2388	1067	< 5.5	1118	1217	61.9	348
Bicalutamide	6828	1452	< 8.6	662	1418	< 8.6	62.3
Clarithromycin	543	12.2	< 7.1	11.1	9.8	< 7.1	< 7.1
Clindamycin	988	10.6	< 7.7	16.0	16.3	< 7.7	< 7.7
Fexofenadine	11154	760	< 8.7	668	730	16.4	209
Propranolol	775	25.6	< 8.1	28.9	22.9	< 8.1	< 8.1
Tramadol	474	290	< 6.5	255	342	25.9	165
Fluconazole	145	166	< 6.4	150	197	15.6	94.4
Diclofenac	538	41.8	< 3.1	11.1	61.9	5.7	34.2
Furosemide	245	16.0	< 7.6	8.7	14.9	< 7.6	< 7.6
Irbesartan	85	48.6	< 7	19.7	53.8	< 7	19.2
Losartan	842	216	< 11	89.9	261	12.1	85.5
Sulfamethoxazole	328	40.9	< 11	43.6	85.4	12.0	48.1
Trimethoprim	221	13.0	< 11	16.0	13.5	< 11	< 11
Erythromycin	1444	513	< 12	666	624	58.5	434
Norsertaline	< 220	< 220	< 220	< 220	< 220	< 220	< 220
Sertraline	63.3	14.2	< 4.9	< 4.9	9.2	< 4.9	< 4.9
Venlafaxine	538	218	< 4.2	292	288	19.5	138
Desvenlafaxine	612	137	< 5.1	179	184	14.3	88.5

Table A.3 (Continued): Concentrations of the selected pharmaceuticals in the filtered effluent and after each treatment step.

Ozone dosage: 0.28 g O₃/ g DOC - Day 12							
Micropollutant	Filtered Effluent	Equalization Tank	GAC	AIX	Reference	Biochar 1	Biochar 2
Atenolol	176	109	< 7.2	127	133	29.7	38.0
Metoprolol	1736	1185	< 7.1	1738	1576	170	431
Carbamazepine	393	91.1	< 5.4	98.9	96.5	67.8	78.9
Cetirizine	255	20.9	< 5.6	24.5	26.2	8.9	19.6
Citalopram	184	23.1	< 4.4	29.2	27.2	< 4.4	5.5
Oxazepam	505	254	< 4.9	261	269	47.2	131
Lamotrigine	1831	887	6.0	973	996	329	514
Bicalutamide	4291	742	< 8.6	485	803	24.6	147
Clarithromycin	540	< 7.1	< 7.1	9.2	11.0	< 7.1	< 7.1
Clindamycin	528	< 7.7	< 7.7	< 7.7	< 7.7	< 7.7	< 7.7
Fexofenadine	5809	473	< 8.7	584	603	110	319
Propranolol	450	< 8.1	< 8.1	< 8.1	< 8.1	< 8.1	< 8.1
Tramadol	585	276	< 6.5	291	237	92.3	184
Fluconazole	159	140	< 6.4	139	122	51.6	112
Diclofenac	521	10.9	< 3.1	8.3	14.9	7.5	20.7
Furosemide	387	< 7.6	< 7.6	< 7.6	< 7.6	< 7.6	< 7.6
Irbesartan	102	32.1	< 7	19.0	34.3	9.4	21.5
Losartan	687	52.8	< 11	33.0	72.7	21.5	49.6
Sulfamethoxazole	211	15.7	< 11	24.9	37.1	13.9	27.0
Trimethoprim	226	< 11	< 11	< 11	< 11	< 11	< 11
Erythromycin	2726	390	< 12	520	538	198	383
Norsertaline	< 220	< 220	< 220	< 220	< 220	< 220	< 220
Sertraline	92.6	17.7	< 4.9	11.4	9.1	< 4.9	< 4.9
Venlafaxine	678	197	< 4.2	255	247	73.4	170
Desvenlafaxine	718	158	< 5.1	203	205	59.7	109

Table A.3 (Continued): Concentrations of the selected pharmaceuticals in the filtered effluent and after each treatment step.

Ozone dosage: 0.96 g O₃/ g DOC - Day 1							
Micropollutant	Filtered Effluent	Equalization Tank	GAC	AIX	Reference	Biochar 1	Biochar 2
Atenolol	346	65.0	< 7.2	61.7	61.8	< 7.2	11.5
Metoprolol	2379	487	< 7.1	561	487	< 7.1	58.9
Carbamazepine	4166	16.7	< 5.4	12.0	14.9	< 5.4	< 5.4
Cetirizine	2381	8.0	< 5.6	< 5.6	7.9	< 5.6	< 5.6
Citalopram	2845	15.2	< 4.4	12.3	13.1	< 4.4	< 4.4
Oxazepam	5152	179	< 4.9	84.3	177	< 4.9	42.8
Lamotrigine	25922	915	< 5.5	715	859	7.3	285
Bicalutamide	19659	350	< 8.6	18.0	322	< 8.6	23.3
Clarithromycin	2119	< 7.1	< 7.1	< 7.1	< 7.1	< 7.1	< 7.1
Clindamycin	3280	< 7.7	< 7.7	< 7.7	< 7.7	< 7.7	< 7.7
Fexofenadine	14250	84.8	< 8.7	52.4	81.3	< 8.7	22.9
Propranolol	2118	< 8.1	< 8.1	< 8.1	< 8.1	< 8.1	< 8.1
Tramadol	4527	157	< 6.5	147	125	< 6.5	50.6
Fluconazole	465	82.5	< 6.4	72.7	68.3	< 6.4	30.7
Diclofenac	405	79.5	89.5	64.5	98.5	83.8	137
Furosemide	1434	< 7.6	< 7.6	< 7.6	< 7.6	< 7.6	< 7.6
Irbesartan	803	22.2	< 7	< 7	24.4	< 7	< 7
Losartan	1322	15.3	< 11	< 11	19.1	< 11	< 11
Sulfamethoxazole	415	15.3	< 11	< 11	19.1	< 11	< 11
Trimethoprim	46.0	27.8	< 11	21.0	27.3	< 11	< 11
Erythromycin	156	< 12	< 12	< 12	< 12	< 12	< 12
Norsertaline	< 220	< 220	< 220	< 220	< 220	< 220	< 220
Sertraline	102	< 4.9	< 4.9	< 4.9	< 4.9	< 4.9	< 4.9
Venlafaxine	13402	88.6	< 4.2	85.2	80.9	< 4.2	26.3
Desvenlafaxine	18508	71.5	< 5.1	68.7	66.1	< 5.1	22.6

Table A.3 (Continued): Concentrations of the selected pharmaceuticals in the filtered effluent and after each treatment step.

Ozone dosage: 0.96 g O₃/ g DOC - Day 5							
Micropollutant	Filtered Effluent	Equalization Tank	GAC	AIX	Reference	Biochar 1	Biochar 2
Atenolol	335	204	< 7.2	48.0	47.9	< 7.2	< 7.2
Metoprolol	1542	1165	< 7.1	417	313	19.3	21.3
Carbamazepine	3185	41.2	< 5.4	< 5.4	6.2	< 5.4	< 5.4
Cetirizine	1833	27.3	< 5.6	< 5.6	< 5.6	< 5.6	< 5.6
Citalopram	1977	46.2	< 4.4	9.1	10.1	< 4.4	< 4.4
Oxazepam	3334	309	< 4.9	107	113	18.1	23.9
Lamotrigine	16776	1366	< 5.5	859	901	211	226
Bicalutamide	17000	609	< 8.6	189	293	17.0	9.2
Clarithromycin	1562	< 7.1	< 7.1	< 7.1	< 7.1	< 7.1	< 7.1
Clindamycin	1979	< 7.7	< 7.7	< 7.7	< 7.7	< 7.7	< 7.7
Fexofenadine	9242	277	< 8.7	73.4	75.2	11.7	14.3
Propranolol	1481	< 8.1	< 8.1	< 8.1	< 8.1	< 8.1	< 8.1
Tramadol	2782	451	< 6.5	69.6	82.0	13.0	21.7
Fluconazole	340	117	< 6.4	52.9	62.7	11.8	20.0
Diclofenac	264	48.3	19.3	15.4	22.2	24.7	26.3
Furosemide	1278	< 7.6	< 7.6	< 7.6	< 7.6	< 7.6	< 7.6
Irbesartan	627	16.3	< 7	13.3	17.8	< 7	< 7
Losartan	791	25.7	< 11	16.9	21.4	< 11	11.9
Sulfamethoxazole	388	25.7	< 11	16.9	21.4	< 11	11.9
Trimethoprim	32.3	46.5	< 11	18.3	17.4	< 11	< 11
Erythromycin	167	< 12	< 12	< 12	< 12	< 12	< 12
Norsertaline	< 220	< 220	< 220	< 220	< 220	< 220	< 220
Sertraline	89.8	20.1	< 4.9	< 4.9	< 4.9	< 4.9	< 4.9
Venlafaxine	9103	288	< 4.2	59.3	57.3	10.8	19.1
Desvenlafaxine	12325	228	< 5.1	44.0	45.3	9.7	15.1

Table A.3 (Continued): Concentrations of the selected pharmaceuticals in the filtered effluent and after each treatment step.

Ozone dosage: 0.96 g O₃/ g DOC - Day 12							
Micropollutant	Filtered Effluent	Equalization Tank	GAC	AIX	Reference	Biochar 1	Biochar 2
Atenolol	387	25.9	< 7.2	15.8	16.9	< 7.2	< 7.2
Metoprolol	1481	127	< 7.1	89.1	104	< 7.1	< 7.1
Carbamazepine	3724	< 5.4	< 5.4	< 5.4	< 5.4	< 5.4	< 5.4
Cetirizine	2335	< 5.6	< 5.6	< 5.6	< 5.6	< 5.6	< 5.6
Citalopram	2446	< 4.4	< 4.4	< 4.4	< 4.4	< 4.4	< 4.4
Oxazepam	3734	93.9	< 4.9	70.2	68.8	< 4.9	13.2
Lamotrigine	17861	840	< 5.5	784	715	35.7	147
Bicalutamide	12520	192	< 8.6	115	161	< 8.6	< 8.6
Clarithromycin	2031	< 7.1	< 7.1	< 7.1	< 7.1	< 7.1	< 7.1
Clindamycin	1581	< 7.7	< 7.7	< 7.7	< 7.7	< 7.7	< 7.7
Fexofenadine	7578	21.2	< 8.7	18.0	17.7	< 8.7	< 8.7
Propranolol	1458	< 8.1	< 8.1	< 8.1	< 8.1	< 8.1	< 8.1
Tramadol	3049	14.9	< 6.5	11.4	12.5	< 6.5	8.6
Fluconazole	344	40.3	< 6.4	28.7	30.7	< 6.4	14.3
Diclofenac	263	117	41.6	29.9	25.4	129	79.1
Furosemide	1212	< 7.6	< 7.6	< 7.6	< 7.6	< 7.6	< 7.6
Irbesartan	777	13.0	< 7	8.0	10.5	< 7	< 7
Losartan	1101	16.4	< 11	< 11	11.9	< 11	< 11
Sulfamethoxazole	110.	< 11	< 11	< 11	< 11	< 11	< 11
Trimethoprim	173	< 11	< 11	< 11	< 11	< 11	< 11
Erythromycin	212	< 12	< 12	< 12	< 12	< 12	< 12
Norsertaline	< 220	< 220	< 220	< 220	< 220	< 220	< 220
Sertraline	139	< 4.9	< 4.9	< 4.9	< 4.9	< 4.9	< 4.9
Venlafaxine	10190	18.5	< 4.2	13.5	14.8	< 4.2	12.4
Desvenlafaxine	13438	11.0	< 5.1	8.6	9.4	< 5.1	8.1

Table A.3 (Continued): Concentrations of the selected pharmaceuticals in the filtered effluent and after each treatment step.

Ozone dosage: 2.17 g O₃/ g DOC - Day 1							
Micropollutant	Filtered Effluent	Equalization Tank	GAC	AIX	Reference	Biochar 1	Biochar 2
Atenolol	304	23.1	< 7.2	21.9	21.8	< 7.2	< 7.2
Metoprolol	1014	97.2	< 7.1	76.2	70.9	< 7.1	< 7.1
Carbamazepine	4548	< 5.4	< 5.4	< 5.4	< 5.4	< 5.4	< 5.4
Cetirizine	2552	< 5.6	< 5.6	< 5.6	< 5.6	< 5.6	< 5.6
Citalopram	2537	< 4.4	< 4.4	< 4.4	< 4.4	< 4.4	< 4.4
Oxazepam	2856	65.9	< 4.9	49.4	67.6	< 4.9	< 4.9
Lamotrigine	12315	660	< 5.5	569	535	< 5.5	40.5
Bicalutamide	10386	136	< 8.6	15.4	185	< 8.6	< 8.6
Clarithromycin	1640	< 7.1	< 7.1	< 7.1	< 7.1	< 7.1	< 7.1
Clindamycin	1573	< 7.7	< 7.7	< 7.7	< 7.7	< 7.7	< 7.7
Fexofenadine	8520	16.5	< 8.7	10.9	16.0	< 8.7	< 8.7
Propranolol	1731	< 8.1	< 8.1	< 8.1	< 8.1	< 8.1	< 8.1
Tramadol	1490	13.9	< 6.5	13.0	12.3	< 6.5	< 6.5
Fluconazole	231	26.6	< 6.4	26.0	24.4	< 6.4	< 6.4
Diclofenac	135	50.6	159	61.0	59.1	92.8	101
Furosemide	551	< 7.6	< 7.6	< 7.6	< 7.6	< 7.6	< 7.6
Irbesartan	939	8.6	< 7	< 7	7.4	< 7	< 7
Losartan	1481	< 11	< 11	< 11	< 11	< 11	< 11
Sulfamethoxazole	119	< 11	< 11	< 11	< 11	< 11	< 11
Trimethoprim	147	< 11	< 11	< 11	< 11	< 11	< 11
Erythromycin	454	19.0	< 12	23.1	19.8	< 12	< 12
Norsertaline	< 220	< 220	< 220	< 220	< 220	< 220	< 220
Sertraline	110	< 4.9	< 4.9	< 4.9	< 4.9	< 4.9	< 4.9
Venlafaxine	7629	19.3	< 4.2	18.9	20.7	< 4.2	< 4.2
Desvenlafaxine	7759	10.8	< 5.1	9.6	10.3	< 5.1	< 5.1

Table A.3 (Continued): Concentrations of the selected pharmaceuticals in the filtered effluent and after each treatment step.

Ozone dosage: 2.17 g O₃/ g DOC - Day 5							
Micropollutant	Filtered Effluent	Equalization Tank	GAC	AIX	Reference	Biochar 1	Biochar 2
Atenolol	310	20.7	< 7.2	20.3	19.0	< 7.2	< 7.2
Metoprolol	922	72.3	< 7.1	67.0	62.6	< 7.1	< 7.1
Carbamazepine	3980	< 5.4	< 5.4	< 5.4	< 5.4	< 5.4	< 5.4
Cetirizine	2261	< 5.6	< 5.6	< 5.6	< 5.6	< 5.6	< 5.6
Citalopram	2449	< 4.4	< 4.4	< 4.4	< 4.4	< 4.4	< 4.4
Oxazepam	2388	51.4	< 4.9	44.7	47.4	< 4.9	6.7
Lamotrigine	11514	607	< 5.5	605	610	7.5	122
Bicalutamide	10683	153	< 8.6	32.5	152	< 8.6	< 8.6
Clarithromycin	1383	< 7.1	< 7.1	< 7.1	< 7.1	< 7.1	< 7.1
Clindamycin	1164	< 7.7	< 7.7	< 7.7	< 7.7	< 7.7	< 7.7
Fexofenadine	7926	14.3	< 8.7	11.6	12.7	< 8.7	< 8.7
Propranolol	1905	< 8.1	< 8.1	< 8.1	< 8.1	< 8.1	< 8.1
Tramadol	1165	9.3	< 6.5	9.0	7.9	< 6.5	< 6.5
Fluconazole	212	21.0	< 6.4	21.8	21.1	< 6.4	< 6.4
Diclofenac	120	51.2	38.9	87.9	39.8	184	134
Furosemide	515	< 7.6	< 7.6	< 7.6	< 7.6	< 7.6	< 7.6
Irbesartan	692	< 7	< 7	< 7	< 7	< 7	< 7
Losartan	1405	< 11	< 11	< 11	< 11	< 11	< 11
Sulfamethoxazole	458	< 11	< 11	< 11	< 11	< 11	< 11
Trimethoprim	< 11	< 11	< 11	< 11	< 11	< 11	< 11
Erythromycin	117	< 12	< 12	< 12	< 12	< 12	< 12
Norsertraline	< 220	< 220	< 220	< 220	< 220	< 220	< 220
Sertraline	110	< 4.9	< 4.9	< 4.9	< 4.9	< 4.9	< 4.9
Venlafaxine	6410	15.0	< 4.2	15.2	13.1	< 4.2	< 4.2
Desvenlafaxine	7231	8.4	< 5.1	8.1	7.3	< 5.1	< 5.1

Table A.3 (Continued): Concentrations of the selected pharmaceuticals in the filtered effluent and after each treatment step.

Ozone dosage: 2.17 g O₃/ g DOC - Day 12							
Micropollutant	Filtered Effluent	Equalization Tank	GAC	AIX	Reference	Biochar 1	Biochar 2
Atenolol	181	< 7.2	< 7.2	< 7.2	< 7.2	< 7.2	< 7.2
Metoprolol	533	37.6	< 7.1	35.2	27.9	< 7.1	< 7.1
Carbamazepine	1133	< 5.4	< 5.4	< 5.4	< 5.4	< 5.4	< 5.4
Cetirizine	764	< 5.6	< 5.6	< 5.6	< 5.6	< 5.6	< 5.6
Citalopram	926	< 4.4	< 4.4	< 4.4	< 4.4	< 4.4	< 4.4
Oxazepam	1046	34.8	< 4.9	34.0	34.6	5.2	8.3
Lamotrigine	6826	442	< 5.5	457	428	111	152
Bicalutamide	6022	93.4	< 8.6	98.6	90.6	9.7	10.3
Clarithromycin	775	< 7.1	< 7.1	< 7.1	< 7.1	< 7.1	< 7.1
Clindamycin	803	< 7.7	< 7.7	< 7.7	< 7.7	< 7.7	< 7.7
Fexofenadine	3032	< 8.7	< 8.7	< 8.7	< 8.7	< 8.7	< 8.7
Propranolol	654	< 8.1	< 8.1	< 8.1	< 8.1	< 8.1	< 8.1
Tramadol	655	< 6.5	< 6.5	< 6.5	< 6.5	< 6.5	< 6.5
Fluconazole	149	15.2	< 6.4	17.0	15.2	< 6.4	7.8
Diclofenac	67.4	50.9	12.8	42.0	19.3	84.3	115
Furosemide	303	< 7.6	< 7.6	< 7.6	< 7.6	< 7.6	< 7.6
Irbesartan	203	< 7	< 7	< 7	< 7	< 7	< 7
Losartan	610	< 11	< 11	< 11	< 11	< 11	< 11
Sulfamethoxazole	316	< 11	< 11	< 11	< 11	< 11	< 11
Trimethoprim	11.5	< 11	< 11	< 11	< 11	< 11	< 11
Erythromycin	132	< 12	< 12	< 12	< 12	< 12	< 12
Norsertaline	< 220	< 220	< 220	< 220	< 220	< 220	< 220
Sertraline	70.8	< 4.9	< 4.9	< 4.9	< 4.9	< 4.9	< 4.9
Venlafaxine	2212	4.3	< 4.2	5.0	< 4.2	< 4.2	4.7
Desvenlafaxine	3733	< 5.1	< 5.1	< 5.1	< 5.1	< 5.1	5.8

Table A.4 : Concentrations of transformation products in the filtered effluent and after each treatment step (Specific ozone dosage: : 0.28 g O₃/ g DOC).

Ozone dosage: 0.28 g O₃/ g DOC - Day 1							
Transformation Products	Filtered Effluent	Equalization Tank	GAC	AIX	Reference	Biochar 1	Biochar 2
Alpha hydroxymetoprolol	128	74.3	<6.2	65.1	64.7	<6.2	14.7
Citalopram related compound E	25.0	13.0	<5.2	19.5	25.4	<5.2	7.3
Fluconazole N-oxide	60.5	<7.6	8.9	<7.6	<7.6	13.1	34.7
4 hydroxy diclofenac	4.6	3.0	<2.6	<2.6	<2.6	<2.6	2.6
4-chloro 5-sulfamoylanthranilic acid	497	390	< 75	364	502	< 75	241
N-demethylerythromycin	< 11	< 11	< 11	< 11	< 11	< 11	< 11
Desvenlafaxine	2665	149	<5.1	142	163	<5.1	48.0
Ozone dosage: 0.28 g O₃/ g DOC - Day 5							
	Filtered Effluent	Equalization Tank	GAC	AIX	Reference	Biochar 1	Biochar 2
Alpha hydroxymetoprolol	137	57.6	<6.2	56.2	60.2	6.2	17.4
Citalopram related compound E	23.1	24.5	<5.2	29.4	39.4	<5.2	11.8
Fluconazole N-oxide	126	<7.6	<7.6	9.8	19.8	31.5	<7.6
4 hydroxy diclofenac	4.6	<2.6	<2.6	<2.6	<2.6	<2.6	<2.6
4-chloro 5-sulfamoylanthranilic acid	713	329	< 75	328	430	188	377
N-demethylerythromycin	< 11	< 11	< 11	< 11	< 11	< 11	< 11
Desvenlafaxine	2945	13.2	<5.1	8.4	12.9	6.2	15.5
Ozone dosage: 0.28 g O₃/ g DOC - Day 12							
	Filtered Effluent	Equalization Tank	GAC	AIX	Reference	Biochar 1	Biochar 2
Alpha hydroxymetoprolol	128	46.3	<6.2	41.0	46.6	10.2	21.1
Citalopram related compound E	22.9	35.1	5.2	29.5	31.0	10.7	15.3
Fluconazole N-oxide	57.1	14.9	<7.6	21.3	9.9	<7.6	<7.6
4 hydroxy diclofenac	5.5	2.8	<2.6	<2.6	<2.6	<2.6	<2.6
4-chloro 5-sulfamoylanthranilic acid	691	346	< 75	282	306	240	240
N-demethylerythromycin	< 11	< 11	< 11	< 11	< 11	< 11	< 11
Desvenlafaxine	3330	6.6	<5.1	8.1	11.2	9.7	15.1

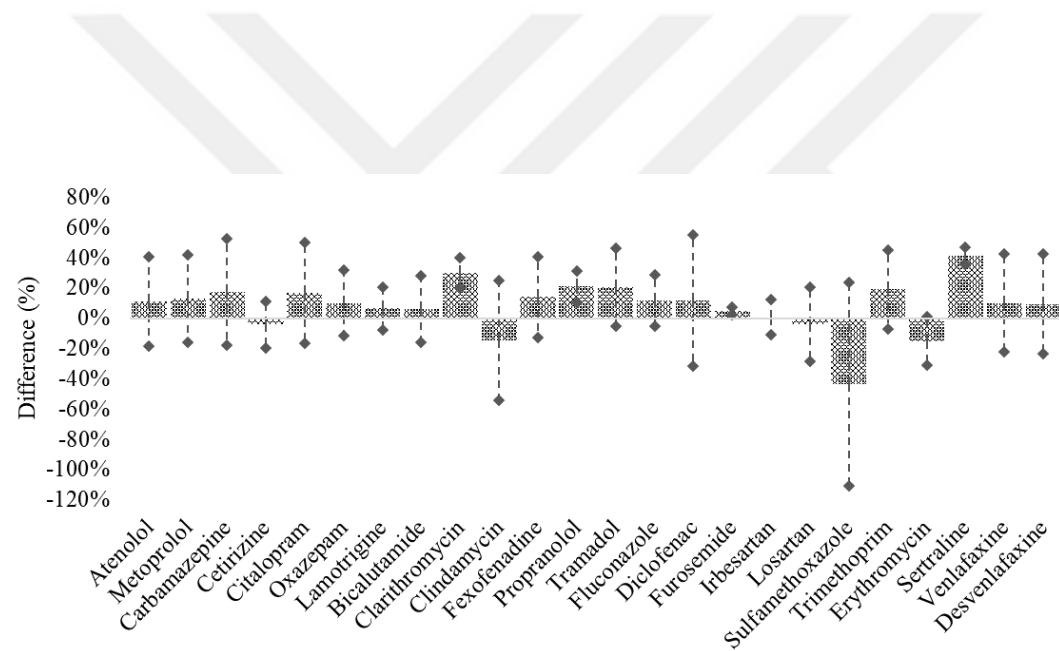


Figure A.1 : The concentration difference between the equalization tank and the reference column as percentage in all samples (n=2-9).

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