T.C.
ISTANBUL UNIVERSITY-CERRAHPASA
INSTITUTE OF GRADUATE STUDIES

M.Sc. THESIS

PRODUCTION AND CHARACTERIZATION OF ORTHOPAEDIC IMPLANT MATERIALS

BERK ATAY

SUPERVISOR
Assoc. Prof. Dr. İlven MUTLU

Department of Nanoscience and Nanoengineering

Nanoscience and Nanoengineering Programme

ISTANBUL- March, 2021

This study was accepted on 8/4/2021 as a M. Sc. thesis in ...., ... by the following Committee.

Examining Committee Members

Assoc. Prof. Dr. İlven MUTLU(Supervisor)
İstanbul University-Cerrahpaşa
Faculty of Engineering

Prof. Dr. Selva ÇAVUŞ
Istanbul University-Cerrahpasa
Engineering Faculty

Assoc. Prof. Dr. Cem KAHRUMAN
Bursa Technical University
Engineering and Natural Sciences Faculty

Academic Title Name SURNAME
University
Faculty

Academic Title Name SURNAME
University
Faculty

As required by the 9/2 and 22/2 articles of the Graduate Education Regulation which was published in the Official Gazette on 20.04.2016, this graduate thesis is reported as in accordance with criteria determined by the Institute of Graduate Sttudies by using the plagiarism software to which Istanbul University-Cerrahpasa is a subscriber.

This thesis is supported by the project numbered 34943 of Istanbul University-Cerrahpaşa Scientific Research Projects Executive Secreteriat.

FOREWORD

I would like to thank my family members who have always supported me in this proces

March 2021 Berk ATAY

TABLE OF CONTENTS

Page

LIST OF FIGURES

Page

LIST OF TABLES

Page

LIST OF SYMBOLS AND ABBREVIATIONS

Symbol	**Explanation**
T	Temperature
t	Time
º	Degree

Abbreviation	**Explanation**
g	Gram
FTIR	Fourier Transform Infrared Spectroscopy
mg	Mili gram
mm	Mili meter
ppm	Parts per million
PEEK	Polyetheretherketone
PVA	Polyvinylalcohol
µm	Micro meter
MA	Mechanical alloying
OCP	Open circuit potential
sPEEK	Sulfonated polyetheretherketone

ÖZET

YÜKSEK LİSANS TEZİ

ORTOPEDİK İMPLANT MALZEMELERİNİN ÜRETİLMESİ VE KARAKTERİZASYONU

BERK ATAY

İstanbul Üniversitesi-Cerrahpasa

Lisansüstü Eğitim Enstitüsü

Nanobilim ve Nanomühendislik Anabilim Dalı

Danışman : Doç. Dr. İLVEN MUTLU

Bu çalışmada, sert doku ortopedik implant uygulamaları (omurga, kalça, diz) için yenilikçi malzemelerin geliştirilmesi, üretilmesi ve karakterizasyonu gerçekleştirilmiştir. Biyomedikal implantlar vücudun işleyişine yardımcı olmak üzere üretilen cansız malzemelerdir. Bu çalışmada artroplasti uygulamaları amaçlı ortopedik implant malzemelerinin geliştirilmesi, üretilmesi, literatür ve birbiri ile karşılaştırılması amaçlanmıştır. Omurga, diz ve kalça uygulamaları için yenilikçi metalik malzemeler (Ta alaşımları) ve yenilikçi polimer malzemeler (sülfonlanmış polietereterketon, sPEEK) geliştirilmiştir. Ta alaşımlarına Nb ilavesi, erime sıcaklığını, elastisite modülünü ve maliyeti düşürmüştür. Sn ve Co ilavesi, Ta alaşımın sinterleme işlemini sıvı faz oluşturarak kolaylaştırmıştır. Ta esaslı alaşımlar mekanik alaşımlama ile hazırlanmıştır. Toz metalurjisi tekniği kullanılarak numuneler üretilmiştir.

Mart 2021, 63. sayfa.

Anahtar kelimeler: Biyomalzeme, ortopedik implant, toz metalurjisi, Ta, PEEK

SUMMARY

M.Sc. THESIS

PRODUCTION AND CHARACTERIZATION OF ORTHOPAEDIC IMPLANT MATERIALS

BERK ATAY

Istanbul University-Cerrahpasa

Institute of Graduate Studies

Department of Nanoscience and Nanoengineering

Supervisor : Assoc. Prof. Dr. İLVEN MUTLU

In this study, novel materials for hard tissue orthopaedic implant applications (spinal, knee, hip) were developed, produced and characterized. Biomedical implants are nonliving devices used in the living body. The aim of this study was development, production and comparison of the orthopaedic implant materials used in arthroplasty (hard tissue) applications. Novel metallic materials (Ta alloys) and novel polymer materials (sulfonated polyetheretherketone, sPEEK) were developed for spinal, knee and hip applications. Nb addition was decreased the melting temperature, elastic modulus and price of the Ta alloy. Sn and Co additions were enhanced the sinterability of the Ta alloy by liquid phase formation during sintering. Ta alloys were prepared by mechanical alloying. The specimens were manufactured by powder metallurgy method.

March 2021, 63. pages.

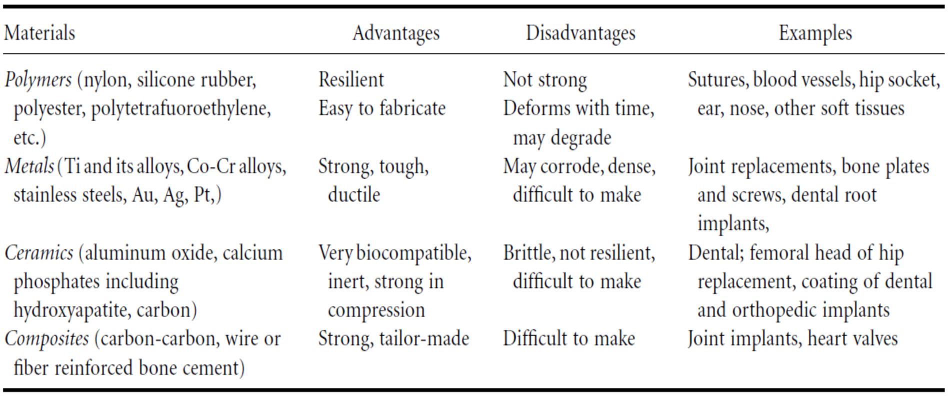
Keywords: Biomaterial, orthopaedic implant, powder metallurgy, Ta, PEEK

1. INTRODUCTION

1.1. BIOMATERIALS

A biomaterial can be defined as a substance that has been engineered to take a form which, alone or as part of a complex system, is used to direct, by control of interactions with components of living systems, the course of any therapeutic or diagnostic procedure. Biomaterials may be natural or synthetic non-living materials and are employed in biomedical applications in order to support, enhance, or replace damaged organ or tissue. In general, the biomaterials are special group of engineering materials. Biomaterials are employed in the production of biomedical implants [1-6]. Large variety of materials are available for implant production. There are metal, ceramic or polymer based biomaterials. Orthopaedic implants (knee, hip) are made by using metal based biomaterials (Ti alloys, CoCr alloys, austenitic stainless stels). Bioceramic (alumina, zirconia) are usually employed as a coatings in wear applications (knee). Biopolymers (PMMA, PEEK, PU, PLA, UHDPE) are employed in soft tissue biomedical applications [1-6]. Biocompatibility is important property for biomedical implant materials. In general, biocompatibility and its opposite property toxicity can be defined as a biomaterial property that contains mechanical, chemical, biomedical, and biological properties. Biocompatibility is a materials property in order to determine the potential toxicity caused from contact with a biomedical implant [1-6].

Table 1.1: Biomaterials used in the body [1]



Materials	Advantages	Disadvantages	Examples
Polymers (nylon, silicone rubber, polyester, polytetrafuoroethylene, etc.)	Resilient Easy to fabricate	Not strong Deforms with time, may degrade	Sutures, blood vessels, hip socket, ear, nose, other soft tissues
Metals (Ti and its alloys, Co-Cr alloys, stainless steels, Au, Ag, Pt,)	Strong, tough, ductile	May corrode, dense, difficult to make	Joint replacements, bone plates and screws, dental root implants,
Ceramics (aluminum oxide, calcium phosphates including hydroxyapatite, carbon)	Very biocompatible, inert, strong in compression	Brittle, not resilient, difficult to make	Dental; femoral head of hip replacement, coating of dental and orthopedic implants
Composites (carbon-carbon, wire or fiber reinforced bone cement)	Strong, tailor-made	Difficult to make	Joint implants, heart valves

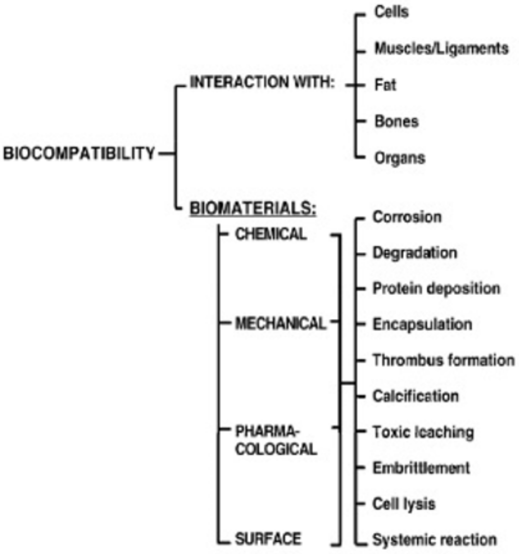
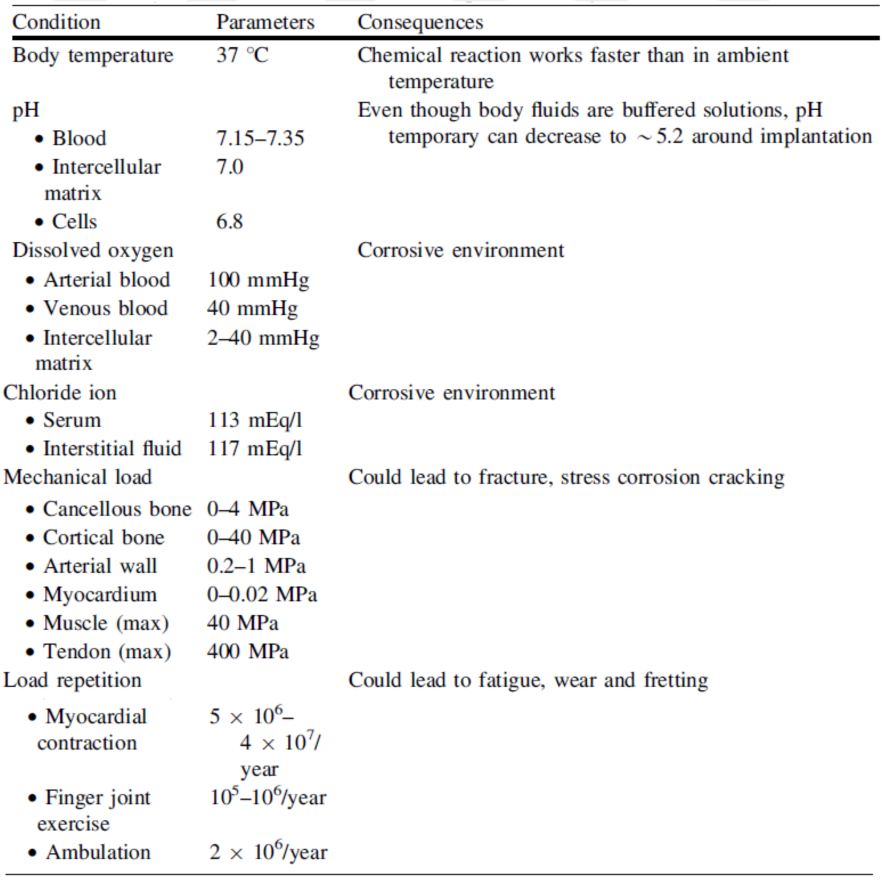


Figure 1.1: Illustration of biocompatibility [1]

Table 1.2: Conditions of the body environments [3]



Condition	Parameters	Consequences
Body temperature	37 °C	Chemical reaction works faster than in ambient temperature
pH		Even though body fluids are buffered solutions, pH temporary can decrease to ~5.2 around implantation
• Blood	7.15–7.35	
• Intercellular matrix	7.0	
• Cells	6.8	
Dissolved oxygen		Corrosive environment
• Arterial blood	100 mmHg	
• Venous blood	40 mmHg	
• Intercellular matrix	2–40 mmHg	
Chloride ion		Corrosive environment
• Serum	113 mEq/l	
• Interstitial fluid	117 mEq/l	
Mechanical load		Could lead to fracture, stress corrosion cracking
• Cancellous bone	0–4 MPa	
• Cortical bone	0–40 MPa	
• Arterial wall	0.2–1 MPa	
• Myocardium	0–0.02 MPa	
• Muscle (max)	40 MPa	
• Tendon (max)	400 MPa	
Load repetition		Could lead to fatigue, wear and fretting
• Myocardial contraction	5×10^6–4×10^7/year	
• Finger joint exercise	10^5–10^6/year	
• Ambulation	2×10^6/year	

1.2. ORTHOPAEDIC IMPLANTS

Compression Screws

In general, bone fracture compression screws (internal fixation devices) can be used in order to fix a bone fracture. In general, fractured bone fragments must be positioned and then internally fixed (stabilized) for until the healing of the bone tissue. Although Ti based lag screws are used, different headless screws have been also developed and employed. In general, the screw can be described as fasten materials/helical devices. The two most common types of screws are cortical bone screw and cancellous bone screw. Bone plates are fixed at a specific place by using compression screws. The fixation of the bone fracture plate on the fractured bone is carried out with the help of compression screws [1, 4-10].

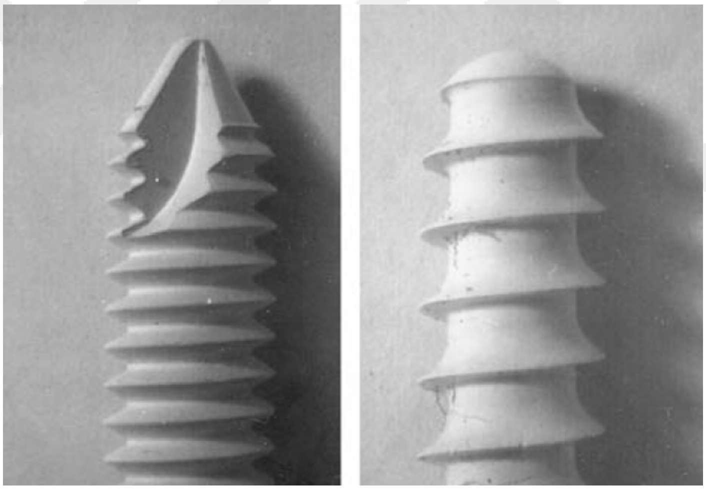


Figure 1.2: Self-tapping bone fracture screw (left), non-self-tapping screw (right). [1]

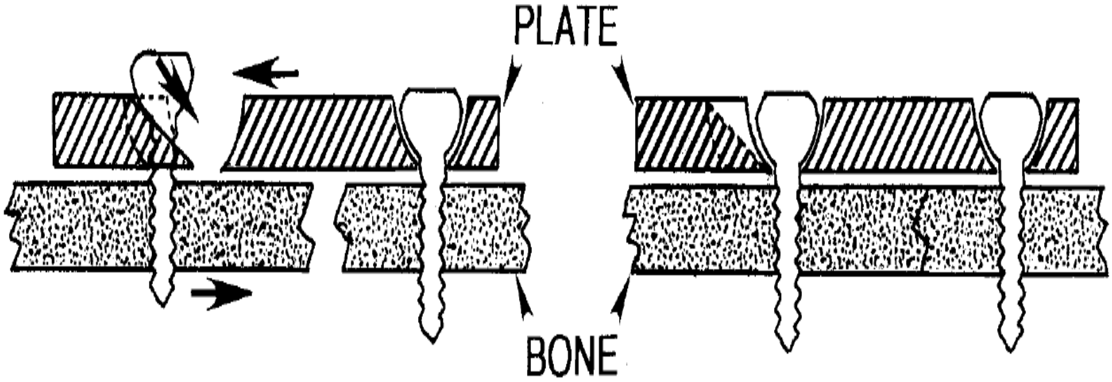


Figure 1.3: Dynamic compression plate theory for fracture fixation. [1]

Anterior Cruciate Ligament (ACL)

ACL is a band of dense connective fibrous soft tissue thant jons 2 neighbour bones (tibia and femur). The microstructure of ACL consists of collagen bundles (type I) and matrix including some proteins and long linear polysaccharide based glycosaminoglycans (GAGs). ACL is a key structure in the knee joint, as it resists anterior tibial translation and rotational loads. ACL is very important for the knee stabilization in humans. There are several temporary impant materials or permanent implant materials (polymers, metals) for replacing the ACL tissue. In general, the ACL keeps the knees stable, which is very important for the human body. ACL provides 85 % of total restraining force of anterior translation. It also prevents excessive tibial medial and lateral rotation, as well as varus and valgus stresses. [4-10].

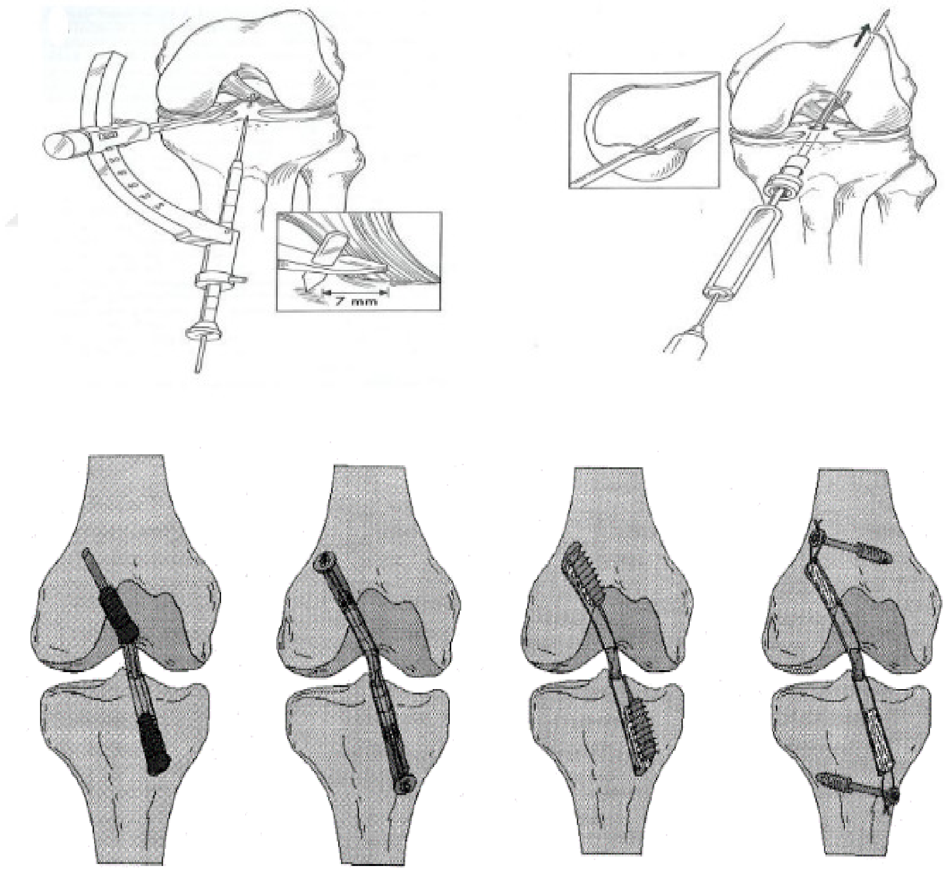


Figure 1.4: Tunneling and fixation [9]

Spinal Implants

Intervertebral disc (IVD) is a very complicated bone-like/cartilage tissue. IVD also known as intervertebla fibrocartilage. The main function of the IVD is to show resistance to external forces/loads in the spine. In general, the IVD provides shock/impact absorption properties to the spine and human body. The spinal column is anatomically defined by the vertebrae, intervertebral discs, ligaments/muscles, and nervous system. IVD is lies between the two neighbour vertebrae. In general, intervertebral discs (IVD) consist of an outer fibrous ring, the anulus fibrosus (AF), which surrounds an inner gel-like center, the nucleus pulposus (NP). The anulus fibrosus (AF) consists of several layers (laminae) of fibrocartilage made up of both type I and II collagen. The disc consists of three zones as AF, NP and cartilage endplates. NP is a gelatinous tissue. Itervertebral disc functions to separate the vertebrae from each other and provides the surface for the shock-absorbing gel of the NP. The NP of the disc functions to distribute pressure in all directions within each intervertebral disc under compressive loads.

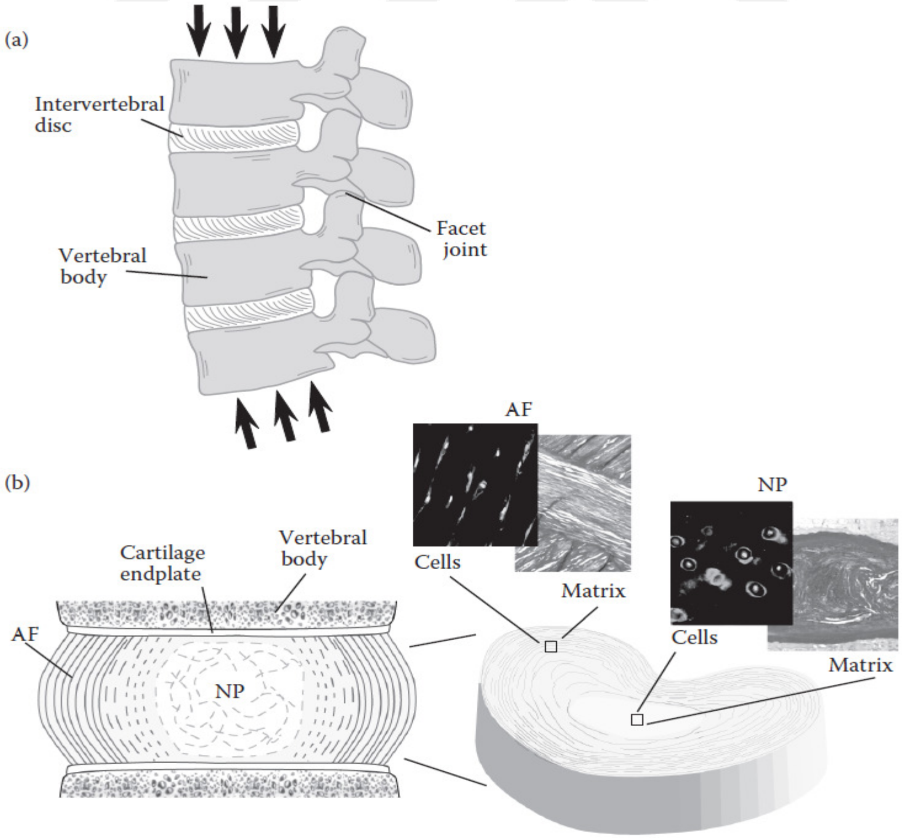


Figure 1.5: a) Intervertebral disc in spinal column, b) zones in disc [6]

The human spinal (vertebral) column, known as backbone, contains 33 vertebrae that are joined by intervertebral discs, ligaments, and facet joint capsules (connective tissue). In general, vertebral column is important in the movement, protects the spinal cord, carry the weight of the body, and forms the axis of the body. There are 5 different regions in the spinal column, each region shows different vertebral structure. Center of gravity of the spinal column is situated about the C2 through the vertebra. C1 (atlas) and C2 (axis) are important for the motion of the head. There are ligaments extending the length of the column at the front and the back, and in between the vertebrae joining the spinous processes, the transverse processes and the vertebral laminae. The vertebral column surrounds the spinal cord which travels within the spinal canal, formed from a central hole within each vertebra. There are different ligaments involved in the holding together of the vertebrae in the column, and in the column's movement. The anterior and posterior ligaments extend the length of the vertebral column along the front and back of the vertebral bodies. The vertebral column is curved in several places, a result of human bipedal evolution. The curves allow the human spine to better stabilize the body in the upright position.

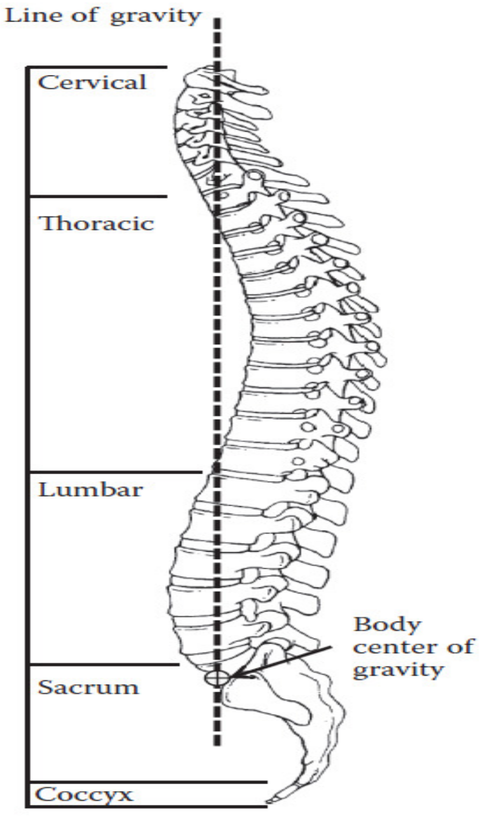


Figure 1.6: Lateral view of spine [6]

Patient Specific Surgary and Patient-Specific Implants (PSI)

Patient-specific orthopaedic implants are promising treatment option for a number of conditions to better match an individual's anatomy. Patient-specific implant (PSI) technology aims to reduce procedural costs, minimize surgical time, and maximize patient outcomes by achieving better biomechanical implant fit. With PSI, computed tomography or magnetic resonance images can be used to create preoperative patient-specific surgical plans and to develop custom cutting guides from 3-D reconstructed images of patient anatomy. Biomedical hard tissue implants (joint arthroplasty) are employed in spine fixation, the joints, tissue reconstruction, fracture fixation. Several factors can cause failure such as motion of the implant due to stress shielding. There is a very high demand to custom made patient specific medicine and patient-specific implants (PSIs) for unique (patient specific) anatomy to enhance the implant life. Custom made patient-specific implants, that is specific to a patient's anatomy, can be manufactured with the help of magnetic resonance imaging (MRI) or tomography (CT) [10].

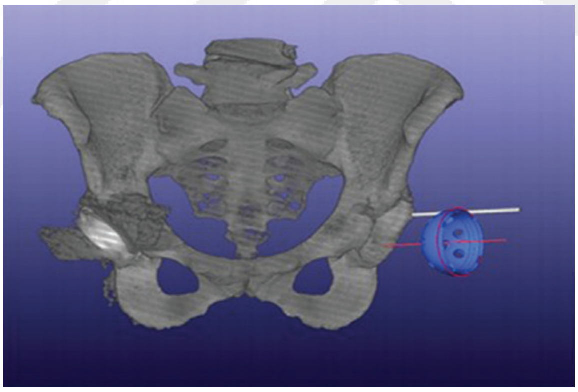


Figure 1.7: Surgical simulation software for patient specific implant (acetabular cup) [10]

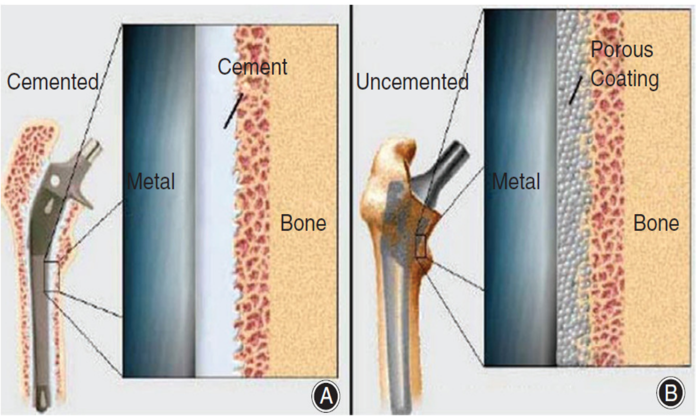


Figure 1.8: a) Cemented implant, b) press-fit implant (cementless) [10]

1.3. TANTALUM

Tantalum is a chemical element with symbol Ta and atomic number of 73. Ta is a rare, hard, easily fabricated, and dark blue-gray metal and was discovered in Sweden by Ekeberg. Ta shows very high electrochemical corrosion resistance. Ta powder can be produced by the Na reduction of the K_2TaF_7 in the hot molten salt. Ta can also be produced by C or Al reduction of its oxide oxide or the hydrogen of $TaCl_5$. The compaction of Ta powder for ingot and processing into final products starts with vacuum arc melting [11-13].

Tantalum exists in 2 crystalline phases, alpha phase and beta phase. The alpha Ta phase is soft and ductile; with body centered cubic structure. The tetragonal beta Ta phase is hard and brittle. The beta Ta phase is metastable and transforms to the alpha phase by heating to 775 °C. Bulk Ta is almost entirely alpha phase, and the beta phase usually exists as thin films.

Tantalum forms compounds in oxidation states −III to +V. Most commonly encountered are oxides of Ta(V), which includes all minerals. Compounds containing Ta are rarely encountered in the laboratory. The metal is highly biocompatible and is used for biomedical implants and coatings.

Ta capacitors are very important in hospital/medical devices. Most important Ta application, (30-35 %), is capacitors. When it is alloyed Ta produces high performance superalloys that allow aircraft engines to operate at very high temperatures. High melting point of Ta (3017 °C) increase the strengthen of the superalloy and enhance the castability. 20-25 % of the produced Ta is used in superalloys manufacturing.

Ta based biomedical implants can be divide into 2 main groups:
1) Ta based capacitors - implantable electronical devices
2) Biomedical implants produced from or coated with Ta

Thin coating of Ta_2O_5 film on Ta is inert to human body fluids, that makes it ideal for biomedical implants. Biomedical Ta implants have been employed in medicine for 50 years without poblems.

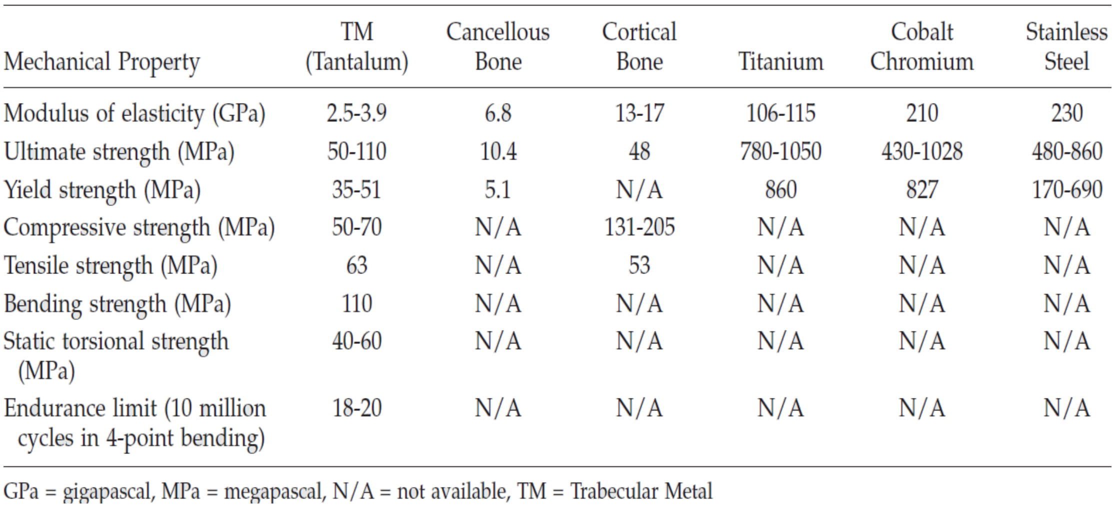
Some medical applications of the Ta:

- total knee/hip implants
- Suture wires
- Sheets/foils and plates for cranioplasty
- Clips (vessels)

As Ta is radiopaque and also bioinert, Ta can be used in the marker balls. These are used in order to track implants (coronary stent) inside the body [11-13].

Porous tantalum is an alternative metal for total joint implants. About 75 % porosity, low elastic modulus, and high wear resistance make it ideal to bone tissue fixation. Ta has very good biocompatibility and is not toxic. The low elastic modulus allows for more physiologic load transfer. Because of its bioactivity, Ta can be employed in total hip implants. Formation of a bone-like apatite film affords strong fibrous ingrowth and allows bone attachment. Production of modular implants also is being developed. Experimental results support studies of porous Ta as alternative implant manufacturing materials [11].

Table 1.3: Mechanical properties of Ta and other metals [11]



Mechanical Property	TM (Tantalum)	Cancellous Bone	Cortical Bone	Titanium	Cobalt Chromium	Stainless Steel
Modulus of elasticity (GPa)	2.5-3.9	6.8	13-17	106-115	210	230
Ultimate strength (MPa)	50-110	10.4	48	780-1050	430-1028	480-860
Yield strength (MPa)	35-51	5.1	N/A	860	827	170-690
Compressive strength (MPa)	50-70	N/A	131-205	N/A	N/A	N/A
Tensile strength (MPa)	63	N/A	53	N/A	N/A	N/A
Bending strength (MPa)	110	N/A	N/A	N/A	N/A	N/A
Static torsional strength (MPa)	40-60	N/A	N/A	N/A	N/A	N/A
Endurance limit (10 million cycles in 4-point bending)	18-20	N/A	N/A	N/A	N/A	N/A

GPa = gigapascal, MPa = megapascal, N/A = not available, TM = Trabecular Metal

Figure given below illustrates the a) highly porous Ta, b) Ta coating on implants, c) failed hip implant, and d) Ta for reconstruction. As the tantalum is radiopaque and nonmagnetic it is very suitable for the biomedical implant applications.

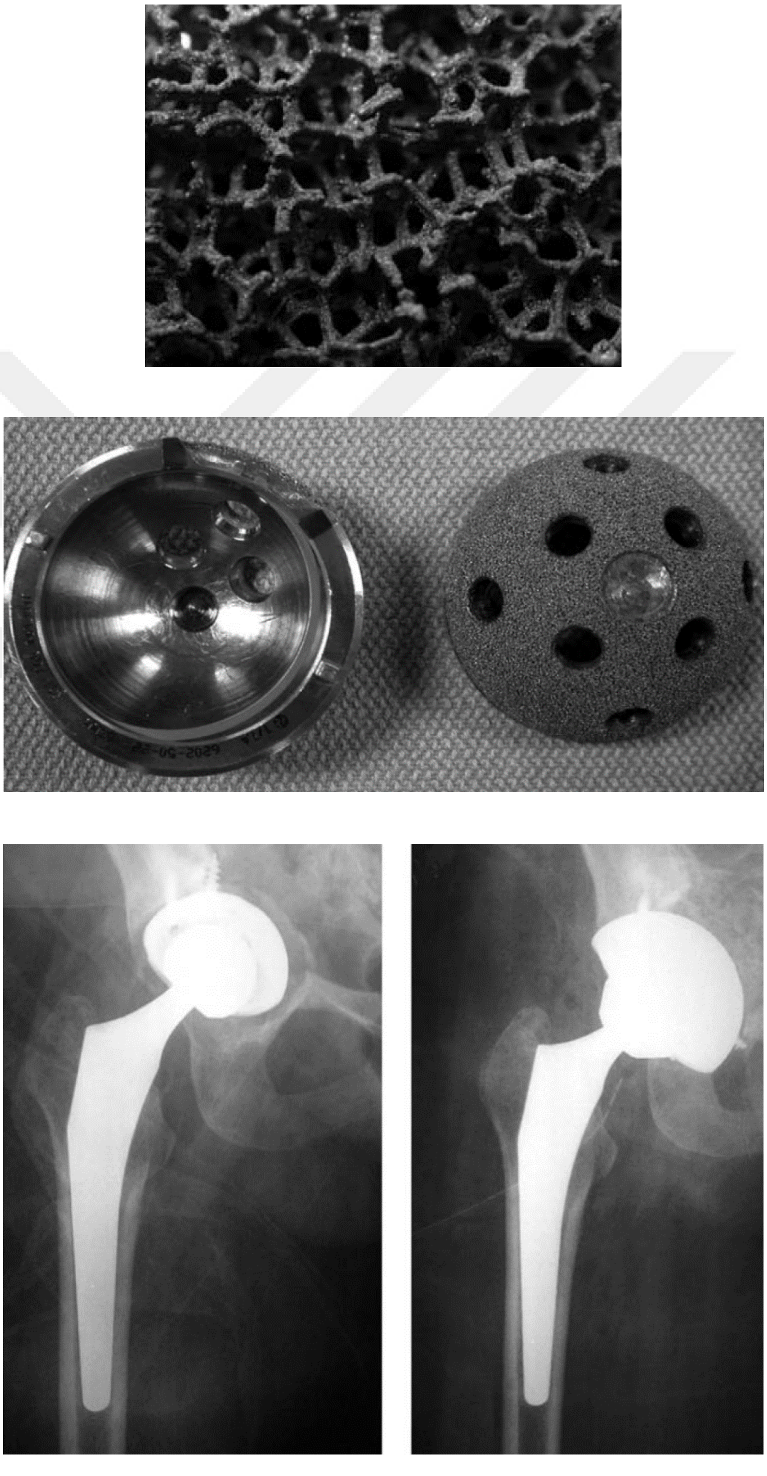


Figure 1.9: a) Porous Ta, b) Ta coating, c) failed hip implant, d) Ta for reconstruction [11]

Figure given below illustrates the images of tantalum in cranio implant, dental implant and knee implant applications. As the tantalum is radiopaque and nonmagnetic it is very suitable for the biomedical implant applications. In addition tantalum shows high biocompatibility and suitable mechanical properties.

Figure 1.10: Ta implants a) cranio, b) dental, c) knee [12]

1.4. POWDER METALLURGY

Powder metallurgy (P/M is an alternative method for casting, plastic deformation, forging, welding. Powder metallurgy (P/M) can be described as technology of manufacturing near-net shape metal components by using fine powders insted of conventional casting and ingot metallurgy. In general, a powder is a granular solid with particle size lower than 1 mm. For conventional powder metallurgy (press-sinter), coarse powder can be defined as powder with size larger than 200 µm [14-16].

Main constraints of the powder metallurgy (P/M) method are;

- Size
- Shape
- Tolerance
- Material
- Properties
- Quantity and Cost

In general, powder metallurgy (PM) can be classified into two main groups: traditional pressing-sintering based methods and advanced methods (full-density processes).

The full-density (advanced PM) methods are;

- Warm (hot) compaction
- Powder forging
- Hot isostatic pressing (HIP)
- Cold isostatic pressing (CIP)
- Powder injection molding (PIM)
- Roll compaction
- Extrusion

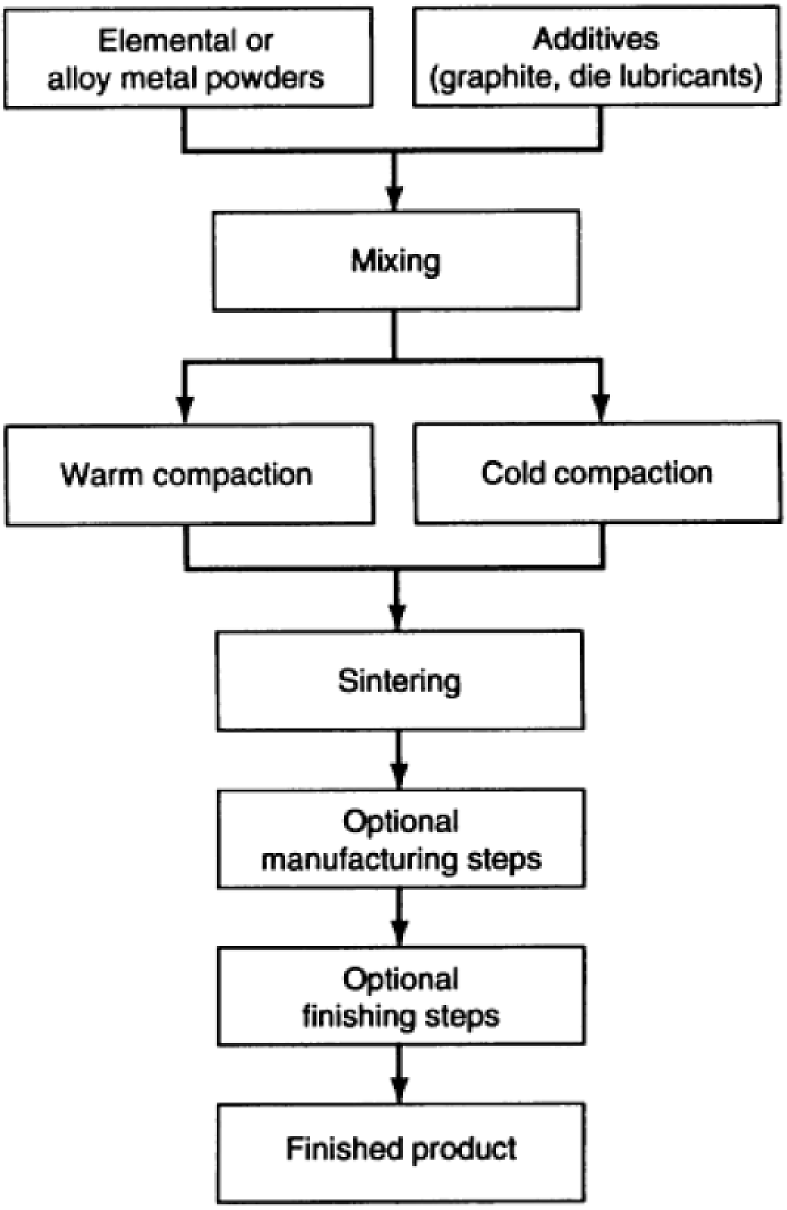


Figure 1.11: Main steps of the powder metallurgy method [16]

Comparison of the Powder Processing Routes

Traditional P/M:

· Alternative materials ca be employed

· Porous parts can be produced. High-porosity filters can be manufactured.

· Relatively lower mechanical properties (residual porosity)

· Relatively cheap process

· Wide range of applications

In order to use traditional powder metallurgy route effectively, the engineer must know the main restrictions of the PM process.

- The product/specimen must be easily ejected from the die
- Need for high strength of the dies and upper/lower punches.

Powder injection molding (PIM):

· Narow range of available materials

· Small and complex geometries

· Wide range in the geometrical complexity

· Expensive process than traditional PM

· High mechanical properties than traditional PM, due to high density [16]

Figure given below illustrates the schematic of press and corresponding density lines inside the specimen (compact). There is no uniform and homogeneous density distribution inside the specimens, especially in the specimens with high heght/diameter ratio.

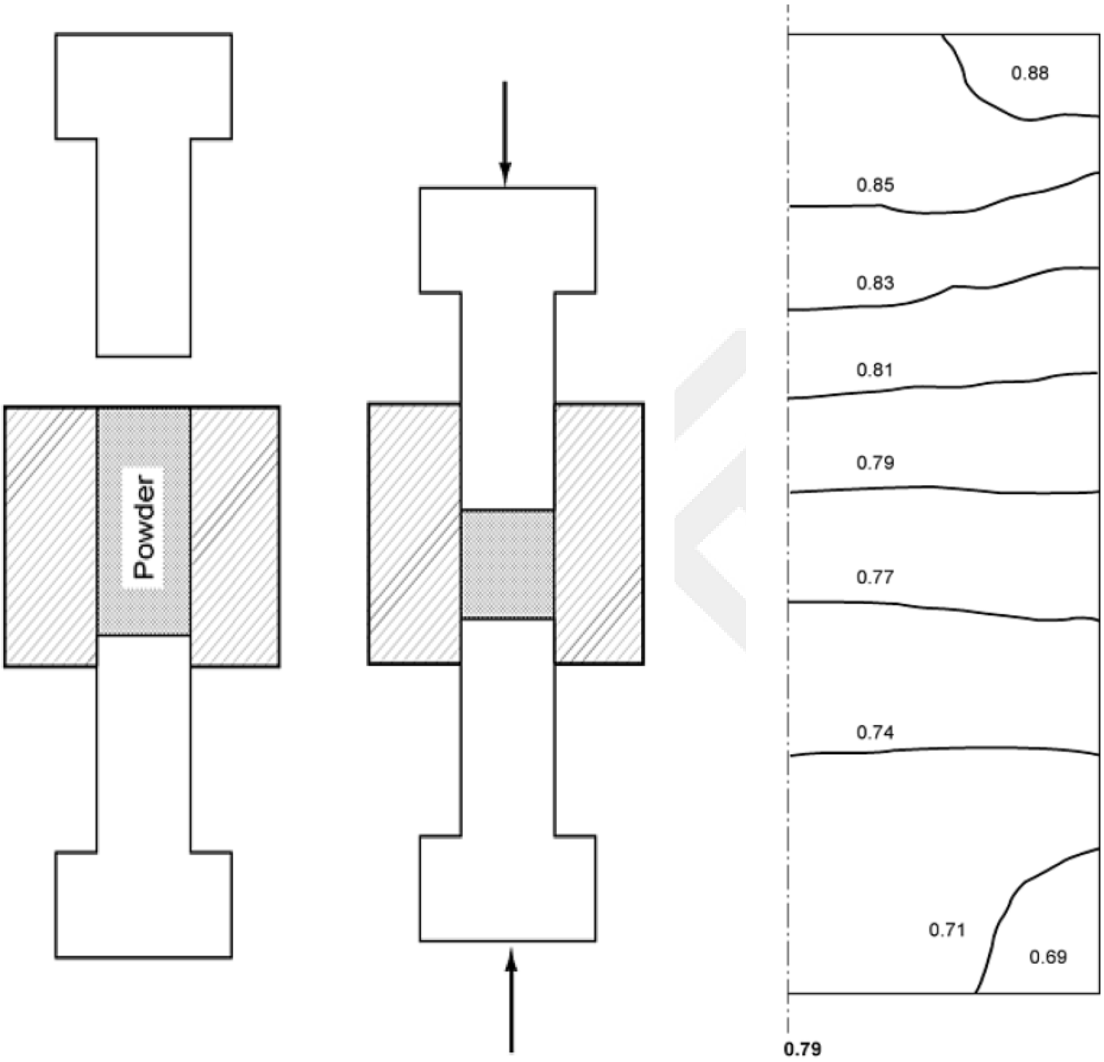


Figure 1.12: Schematic of press and corresponding density lines [16]

Sintering is very important process in the obtaining of high density, high strength and compacted products by forming strong bonds between particles. The sintering temperature is always lower than melting temperature of the main metal (element) and there is no melting in the sintering process.

In general, sintering can be described as a type of heat treatment. Sintering process occurs in a series of steps, depend on temperature and time. Sintering is a high-temperature process that consolidates and strengthens compacted powders into a dense product. During the high temperature sintering process the metal powder particles bonds together and densify by the shrinkage of the pores.

Sintering stages:

- Initial bonding between metal particles
- Growth of the interparticle necks
- Closure of the large pore channels
- Rounding of the pores
- Pore shrinkage (densification)
- Coarsening of the small pores

Sintering parameters

- Heating/cooling rate
- Temperature
- Time
- Furnace atmosphere

Material transport in the PM process

- Viscous flow
- Grain boundary diffusion
- Evaporation/condensation
- Surface diffusion
- Lattice/volume diffusion

1.5. LITERATURE REVIEW

Kim et al. [17] studied the compaction properties of Ta powders during pressing and sintering, The authors were characterized the sintered specimens. Densification properties of the Ta powders are investigated based on the yield properties. Density distribution for larger powders is homogeneous because large particles exhibits higher tap density (lower friction between powders). Cold isostatic pressing (CIP) method is capable of manufaturing denser parts than the traditional pressing-sintering method.

Adamek et al. [18] introduced an interesting method of the highly porous Ta foam biomaterial manufacturing with sucrose crystals (space holde), and subsequent induction heating sintering step. Sucrose crystals have been employed. Influence of the total amount of sucrose powder on the total porosity of the Ta spcimens was investigated. In general, Ta foams were manufactured in the 50-70 % porosity range. Sucrose has a important effect on the phase composition. The study shows TaC formation during the high temperature (sintering). Increase of the pore content lowered the mechanical properties.

Ruperez et al. [19] studied the production of the highly porous Ta scaffolds by using the space holder route. The effects of of space holder NaCl powders, and pressing force on specimen structure and general mechanical properties were studied. The investigation of the Ta based specimens was carried out by using SEM, CT, and intrusion porosimetry methods. This production method was allowed inter-connected Ta structure (about 70 % porosity) and elasticity value close to human bone tissue.

Wang et al. [20] studied fabrication of highly porous Ta-Nb specimens by using traditional powder metallurgy based sponge impregnation route. Highly porous specimens showed interconnected pore structures with about 60-65 % pore content. Highly porous specimens showed sintering neck growth, and more shrinkage of the micropores, with raising Nb contents. In general, the Ta based specimens were not show cytotoxicity. Meanwhile, the Ta based specimens were showed suitable biocompatibility for medical usage.

Kim et al. [21] studied the fabrication of a powder metallurgy based Ta samples with full density and by using isostatic compaction (HIP/CIP) routes. Raising the density and make the homogeneous density, cold isostatic pressing of Ta powders was conducted. Before the HIP, CIP samples were degassed. Then, HIP was carried out on the specimens for full densification. Effect of manufacturing parameters was studied. Strength was raised with raising grain size. This was attributed to the oxygen level of the samples.

Kurtz et al. [22], studied polyaryletherketones (PAEKs) as biomaterials for trauma, orthopedic, and spinal implants. This family of polymers is strong, inert, and biocompatible. Due to its relative inertness, PEEK biomaterials are an attractive platform upon which to develop novel bioactive materials, and some steps have already been taken in that direction, with the blending of HA and TCP into sintered PEEK. However, blended HA-PEEK composites have involved a trade-off in mechanical properties in exchange for their increased bioactivity. PEEK has had the greatest clinical impact in the field of spine implant design, and PEEK is accepted as a radiolucent alternative to metallic biomaterials in the spine community. For mature fields, such as total joint replacements and fracture fixation implants, radiolucency is an attractive but not necessarily critical material feature.

2. MATERIALS AND METHODS

2.1. PRODUCTION OF POLYMER MATERIALS

Additive Manufacturing (AM)

3D printing, or additive manufacturing (AM), is the construction of a three-dimensional object from a CAD model. Additive manufacturing builds parts layer by layer by depositing material according to digital CAD model. In this thesis, firstly the additive manufacturing method was used in order to produce prototypes/specimens. The prototypes (vertebrae and intervertebral disc) were produced by a additive manufacturing device (Formlabs). The additive manufacturing (rapid prototyping) device was stereolithography based. Photopolymer (acrylic based) was employed as a raw material. UV light source was scanned layer by layer by the mirror system to selectively cure (photopolimerization) the polymer.

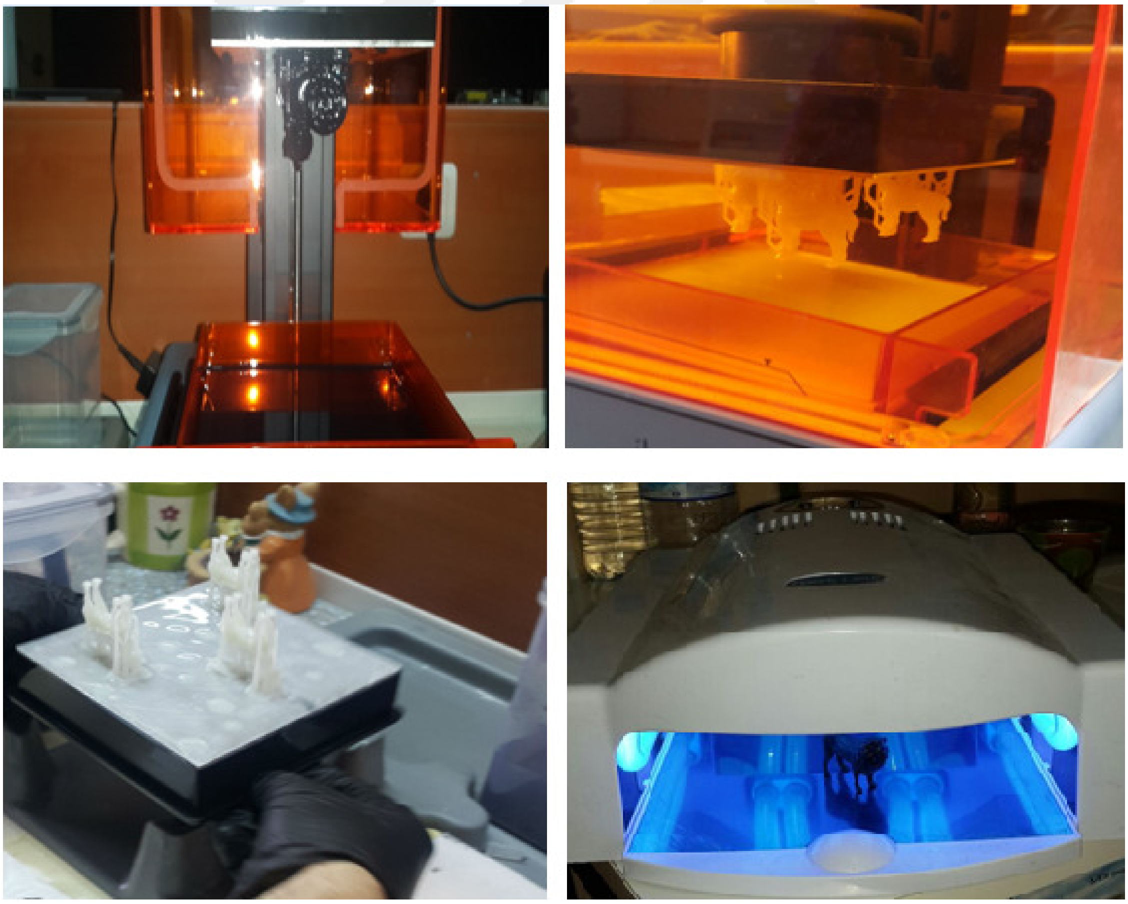


Figure 2.1: Stereolithography based rapid prototyping method

PEEK Specimens

Polyetheretherketone (PEEK) is a thermoplastic polymer, used in the engineering applications. It was originally introduced by Victrex PLC, then imperial chemical industries (ICI) in the early 1980s. PEEK is a semicrystalline thermoplastic with excellent mechanical and chemical resistance properties that are retained to high temperatures. Its elastic modulus is 3.6 GPa and its tensile strength is 100 MPa. PEEK has a glass transition temperature of 143 °C and melts around 343 °C. Some grades have a useful operating temperature of up to 250 °C. PEEK based specimens were produced by traditional powder metallurgy method (pressing-sintering). PEEK based composite specimens were produced by high purity fine PEEK powders with average size of 80 µm (GoodFellow, England). PEEK powders and additives (Fe, Sn, TCP ($Ca_3(PO_4)_2$), alumina (Al_2O_3) powders) were mixed (5 wt. %) and then the mixture was compacted. Lastly the polyetheretherketone (PEEK) based sample was sintered at 340 °C for 1 hour.

Figure 2.2: PEEK based specimens

Table 2.1. Density values of the green and sintered PEEK specimens

	Green density (g/cm^3)	**Sintered density (g/cm^3)**
Pure PEEK	1.26	1.30
PEEK-Fe	1.63	1.66
PEEK-TCP	1.48	1.55
PEEK-Al_2O_3	1.50	1.56
PEEK-Sn	1.59	1.64

Sulfonation Surface Treatment

Figure given below illustrates the main steps of the sulfonation surface treatment of the PEEK samples. Sulfonation surface treatment of the PEEK specimens was carried out in stirred concentrated sulfuric acid (98 wt.%) at room temperature for about 5 minutes. This surface treatmen was employed in order to obtain SO_3H (hydrophilic) groups at the surface and then enhance the wettability and bioactivity of the PEEK based samples. Also, microporous surface structure was obtained by sulfonation surface treatment on the sulfonated PEEK (sPEEK).

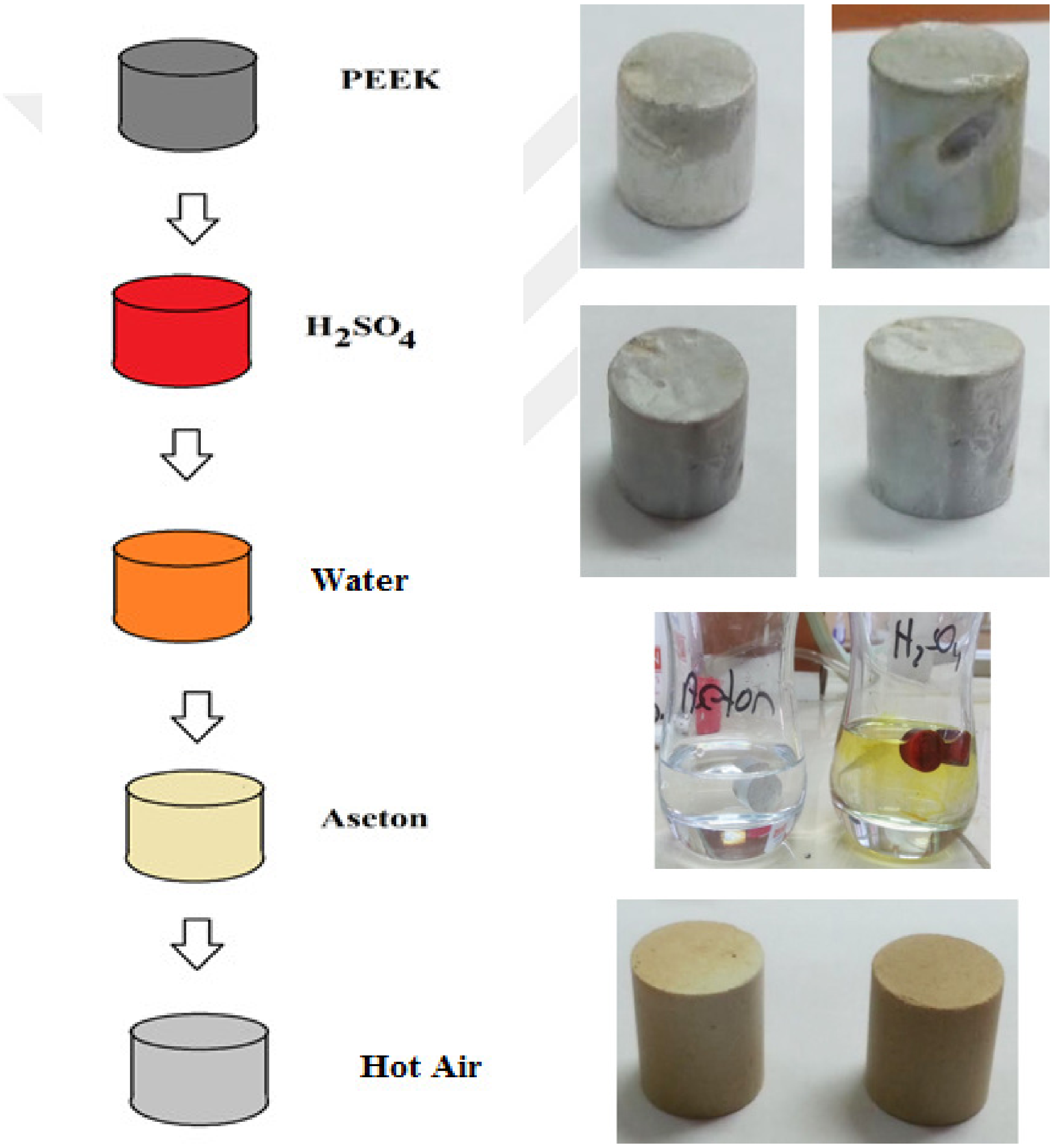


Figure 2.3: Sulfonation surface treatment of PEEK specimens

2.2. PRODUCTION OF METAL ALLOYS

Powder Metallurgy (PM) Method

Powder metallurgy can be described as technology of manufacturing metal components by using fine powders insted of conventional casting and ingot metallurgy. In the experiments, the Ta based alloy specimens were manufactured by using fine metal powders with average particle sizes of 30-40 µm (Alfa Aesar, USA). Ta based green specimens were produced by the following steps: metal powder mixing step, alloy preparation by mechanical alloying (ball mill), and pressing step at about 200-50 MPa. Then, the sintering process of the green Ta alloy specimens at about 1400 ºC was carried out for 120 minutes under vacuum atmosphere to prevent the oxidation. Table given below shows the compositions of the alloys.

Table 2.2: Compositions of the Ti-Ni based alloys

Alloy	**Co**	**Sn**	**Nb**
Ta-Co	1-5		
Ta-Sn		1-5	
Ta-Nb			1-35
Ta-Nb-Sn		1-5	1-35
Ta-Nb-Co	1-5		1-35
Ta-Nb-Co-Sn	1-5	1-5	1-35

Figure 2.4: a) Ball mill and hydraulic press, b) sintering furnace

Powder Injection Moulding (PIM) Method

Powder injection moulding (PIM) is a means of mass-producing various metal or ceramic 3-dimensional components in large production quantities at low costs. In this method, cylindrical product was manufactured by using injection-molding machine (MSE, Turkey). Polymer based binder system, which is important for mouldability/flowability, was consisted of 35-40 wt. % wax (paraffin), 60-65 wt. % polyethylene (PE). The final mixture was included plastic binder (35-40 %) and metal powders (60-65 %). Injection temperature of the process was 185 ºC. Polymers were removed by using heated hexane (for paraffin) and heating (for PE). Lastly, the samples were sintered at 1400 ºC for 120 minutes under vacuum.

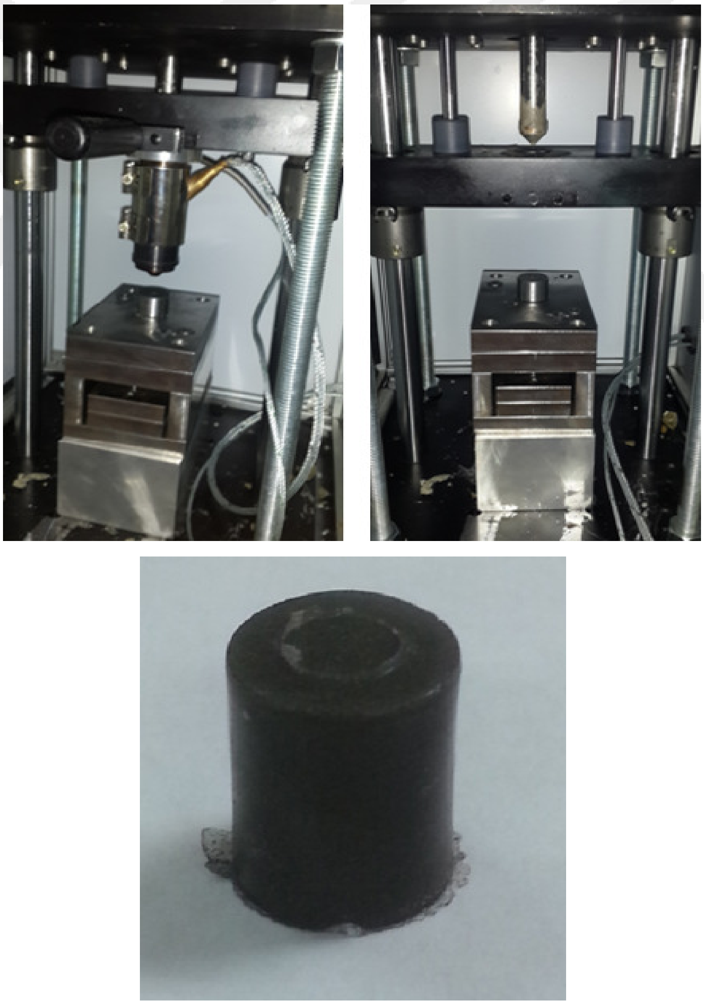


Figure 2.5: Powder injection molding method

2.3. CHARACTERIZATION

Microstructure and Mechanical Properties

The SEM device was employed in order to investigate the microstructure (pore morphology, pore size and microstructural phases) of the specimens (FEI Quanta FEG 450). Densities (% porosity) were determined by using gravimetric (geometrical) method. X-ray diffraction (Rigaku 2200) was used for the identification and evaluation of the phases in the microstructure of the alloys.

Wettability (contact angle) of the samples was studied by using optical tensiometer-contact angle meter (Attension Theta) by the sessile drop method. 5 mL water droplets were dropped on the samples at three different positions. Static contact angle was defined by fitting the Young-Laplace equation around the droplet.

Mechanical properties (elastic modulus and compressive strength) of the samples was examined by performing tension-compression tests (Devotrans, Turkey). Hardness values of the polymers were measured by Shore D durometer (Devotransi Turkey).

Figure 2.6: Tension-compression test device

Static Immersion Tests and Electrochemical Corrosion Tests

The simulated body fluid (SBF) solution was prepared by using following chemical reagents.

- 8.00 g/L NaCl
- 0.30 g/L $CaCl_2$
- 0.20 g/L KCl
- 0.30 g/L $MgCl_2$
- 0.20 g/L K_2HPO_4
- 0.35 g/L $NaHCO_3$
- 0.07 g/L Na_2SO_4

The pH level of the simulated body fluid (SBF) solution was set to 7.40 value by using 0.1 g/L Tris. The Ta alloys were immersed into the SBF up to 14 days. The ICP-MS (Thermo Scientific) was employed in order to find the Ta release levels. Weight change values were determined by dry weight measurements.

Electrochemical corrosion tests were carried out in the simulated body fluid environment by using a potantiostat (Gamry, Interface 1000). Saturated calomel electrode (SCE) was used as reference electrode. Graphite rod was used as a counter electrode (cathode). Ta alloy sample was used as working electrode (anode). OCP (open circuit potential), Tafel, and linear polarization resistance (LPR) methods were employed to determine the corrosion behaviour of the Ta specimens.

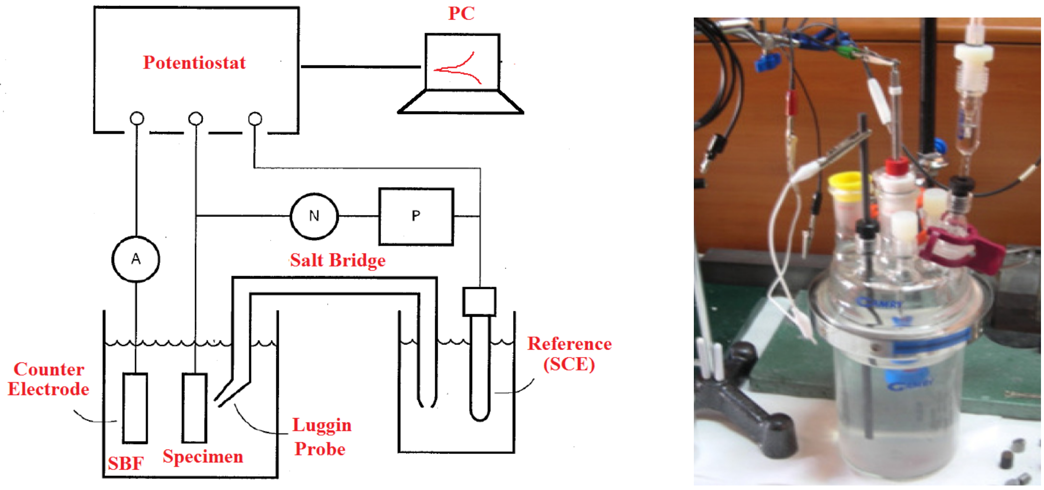


Figure 2.7: Electrochemical corrosion test set-up

3. RESULTS

3.1. POLYMER MATERIALS

Microstructure

Vertebral interbody lumbar cage (intervertebral disc) and lumbar vertebra prototypes were produced by additive manufacturing device (3-d printer). Figure given below shows the photographs of the (a) vertebral interbody lumbar cage prototypes (left: polymer matrix composite specimen, right: acrylic resin prototype), and (b) lumbar vertebra (body) prototypes (views from up and down).

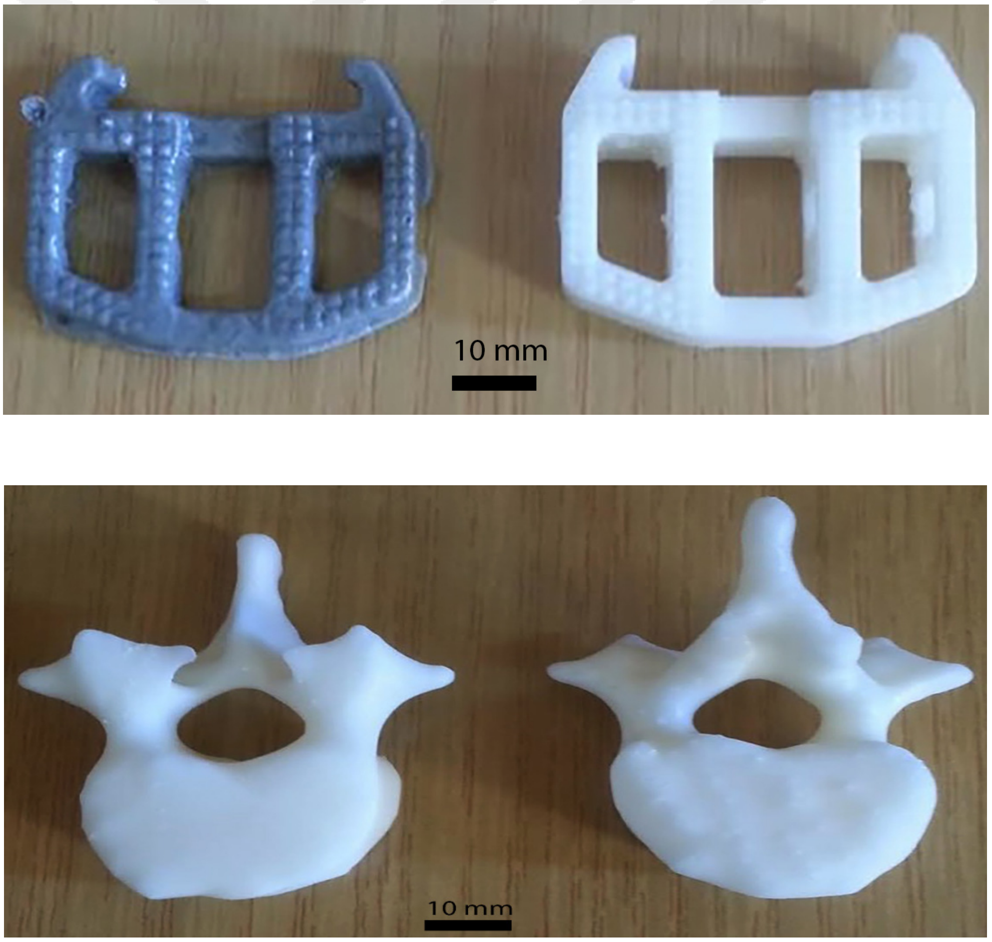


Figure 3.1: Photographs of (a) interbody lumbar cage (b) lumbar vertebra (body) prototypes

Figure given below shows the scanning electrone microscopy (SEM) pictures of the fine PEEK powder, Fe powder and the microstructure of the sintered PEEK-Fe polymer matrix composite specimen. There is a suitable sintering, and there is no defects cracks and macropores in the microstructure of the sintered PEEK based specimens.

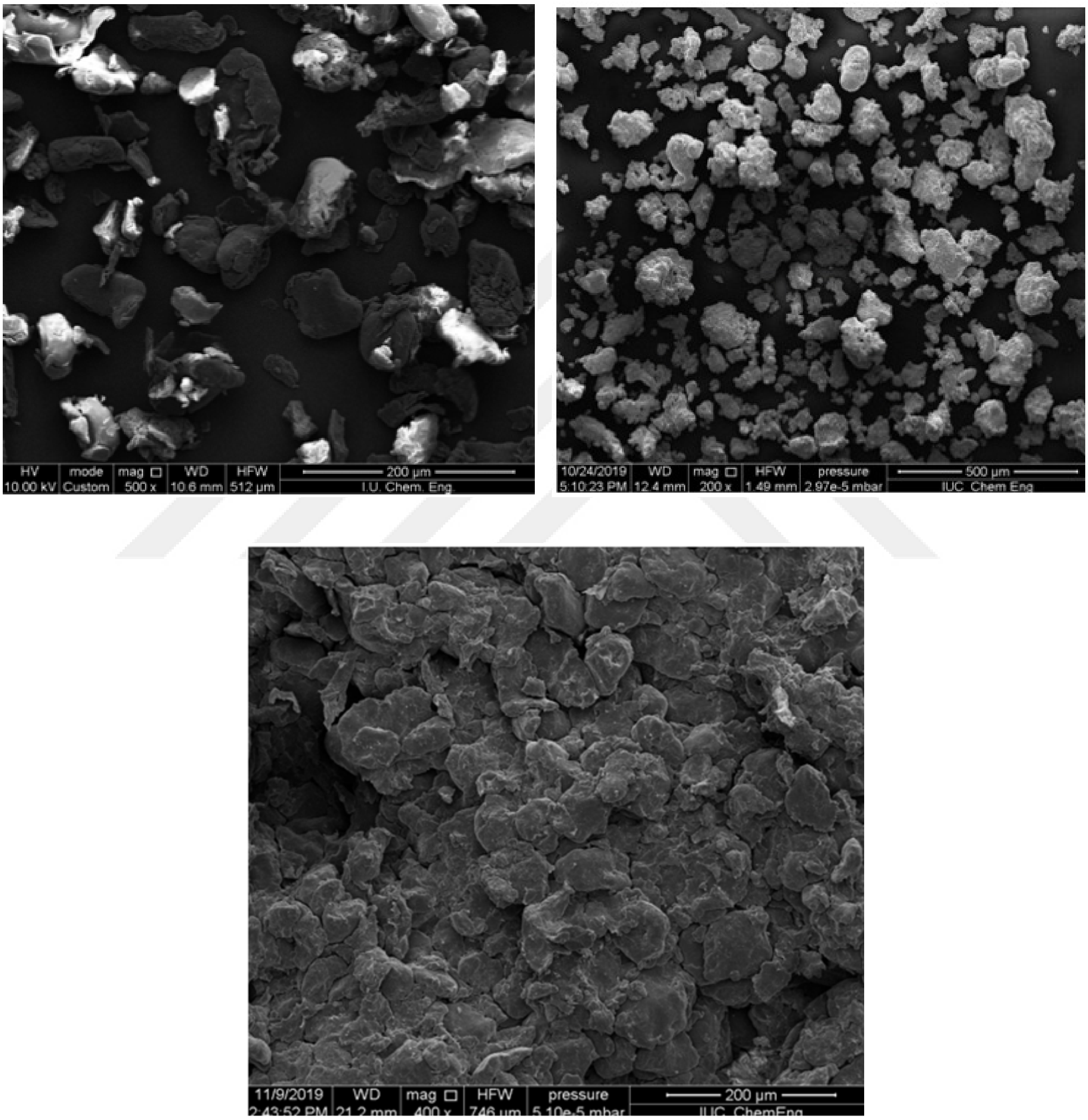
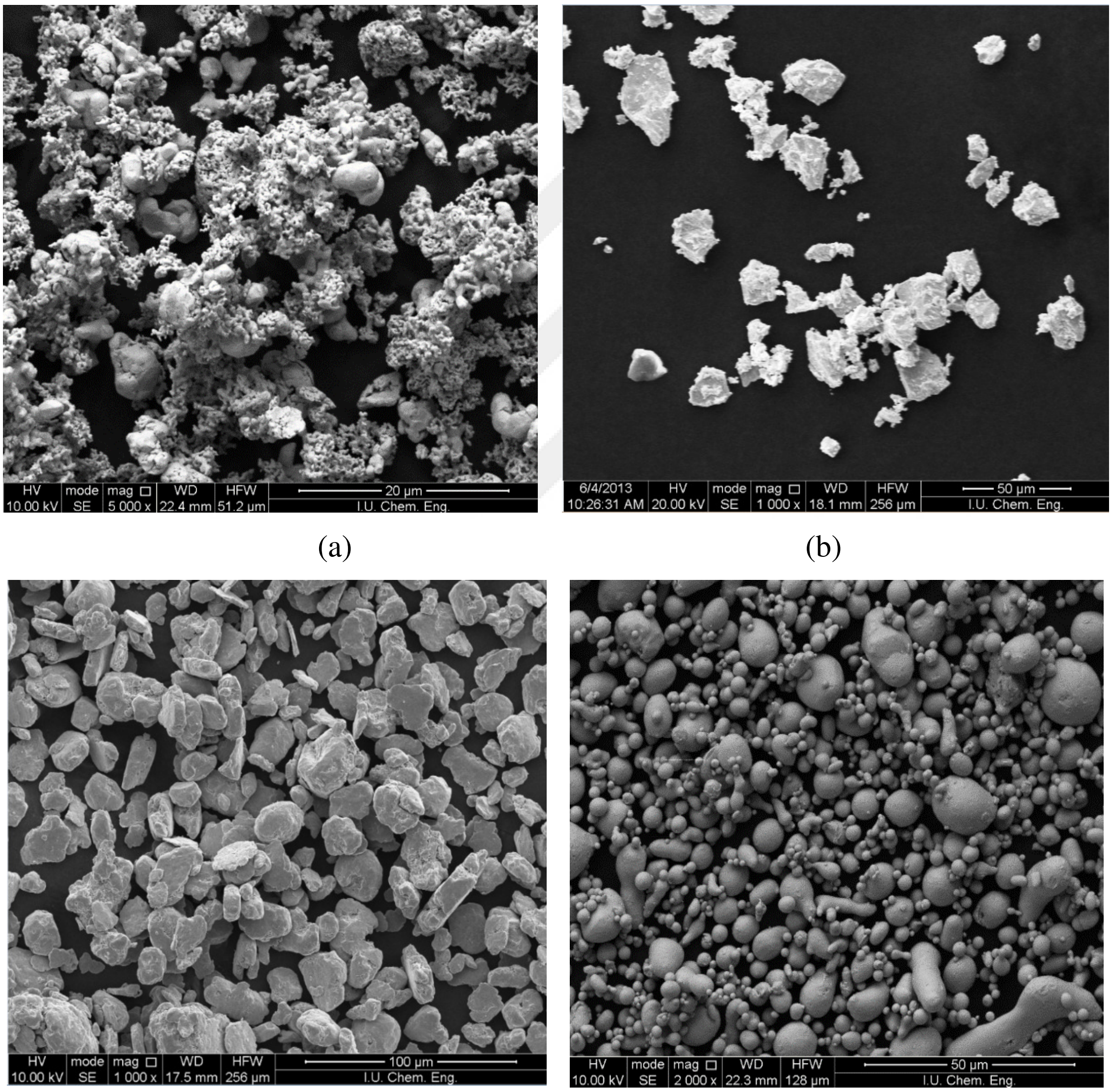


Figure 3.2: SEM pictures of a) PEEK powder, b) Fe powder and c) PEEK-Fe specimen

3.2. METAL ALLOYS

Microstructure

Ta based specimens were manufactured by traditional powder metallurgy (P/M) method by using fine metal powders. Figure given below exhibits the SEM pictures of the (a) Ta powder, (b) Nb powder, (c) Co powder, (d) Sn powder.



(a) (b)

(c) (d)

Figure 3.3: SEM picture of a) Ta, b) Nb, c) Co, d) Sn powders

Figure given below shows the SEM picture of the sintered Ta alloy specimen. As seen from the figure given below, there is a suitable sintering between the metal powder particles. As seen from the images, there is no microcracks/macrocracks or large defects in the microstructure of the sintered Ta alloy samples.

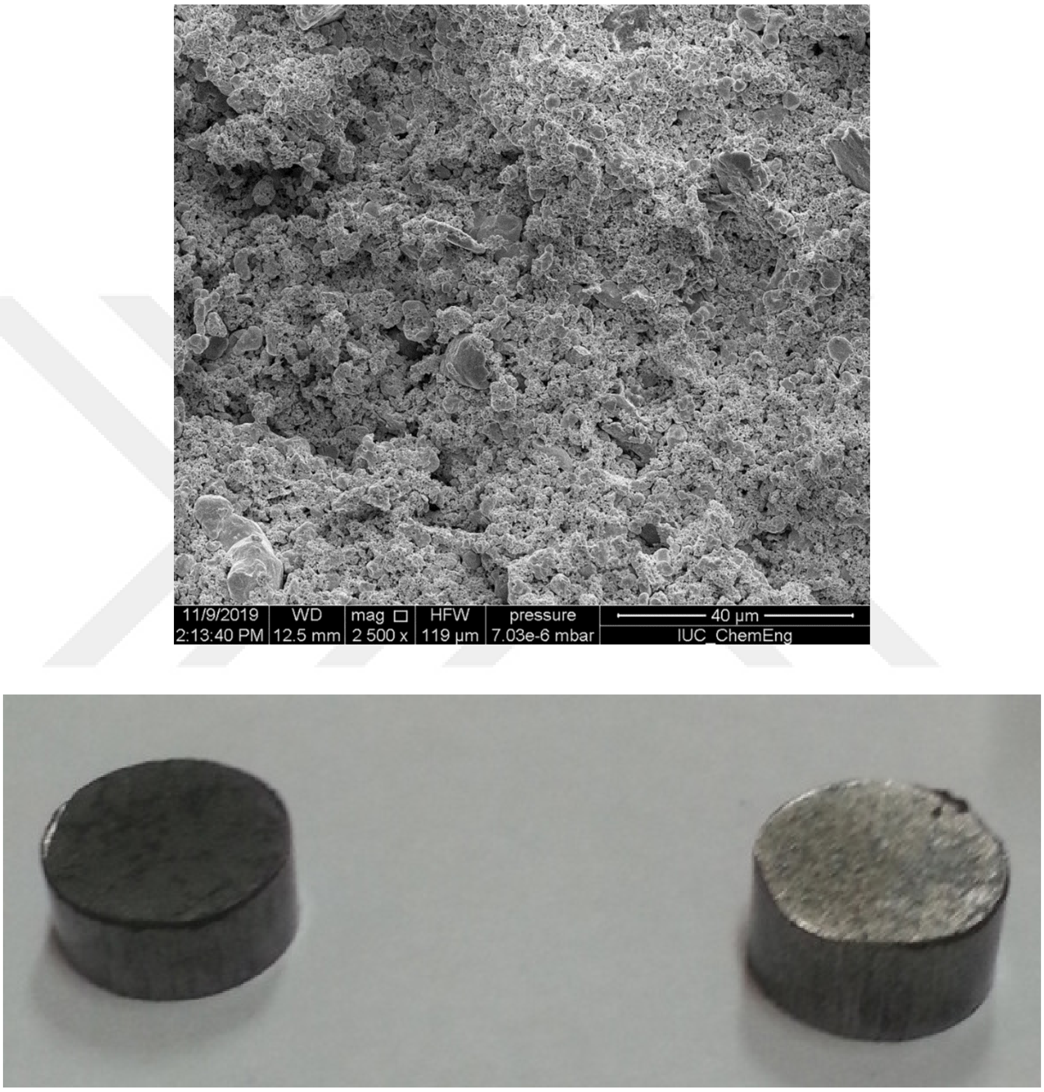


Figure 3.4: a) SEM picture of microstructure, b) photograph of sintered Ta alloy

XRD Results

Microstructure of the Ta based alloys was also characterized by the x-ray diffraction (XRD) study. Figure given below shows the x-ray diffraction (XRD) results of the Ta based alloy and metal powders (additives). Figure given below illustrates the x-ray diffraction (XRD) graph of the powders (a) Ta powder, (b) Nb powder, (c) Sn powder and (d) sintered Ta-Nb-Sn alloy. As-received Ta powders was consisted of Ta phase. The sintered sample was consists of Ta phase. Some oxides (Ta_2O_5 and Nb_2O_5) were also observed on the surfaces of the sintered Ta based alloys.

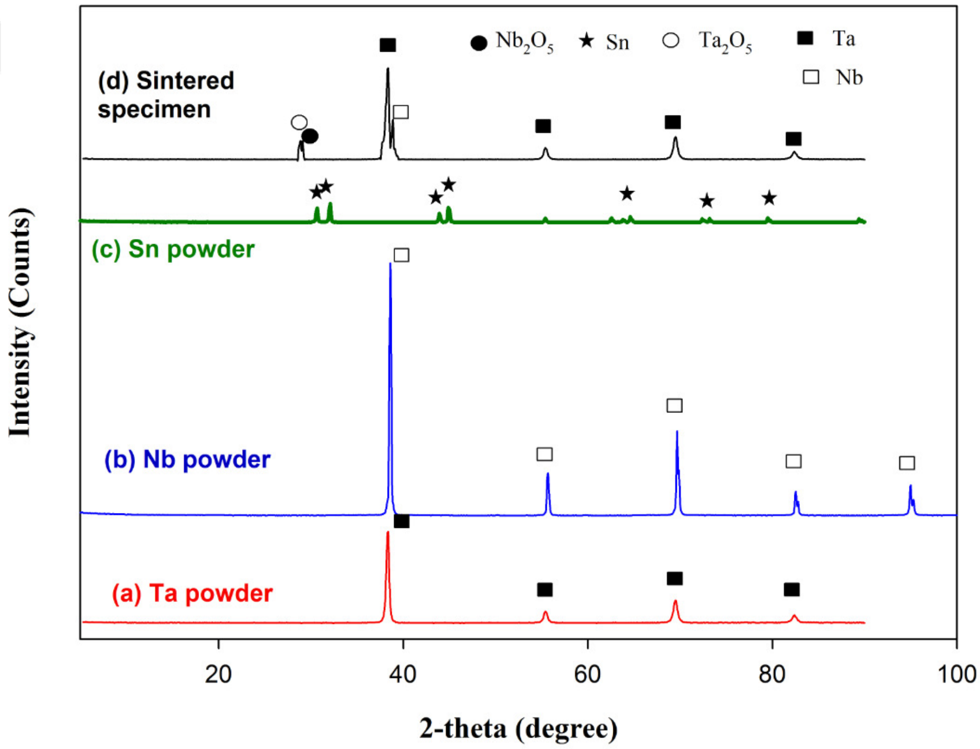


Figure 3.5: XRD results of the alloys

Electrochemical Corrosion Tests

Figure given below illustrates the change of the open circuit potential (OCP) level of the sintered Ta based specimens with the (a) Nb addition and (b) Sn addition. Raising the Nb content of the Ta alloy sample was increased the open-circuit potential (OCP) level, while increasing Sn content was slightly lowered the OCP of the specimens.

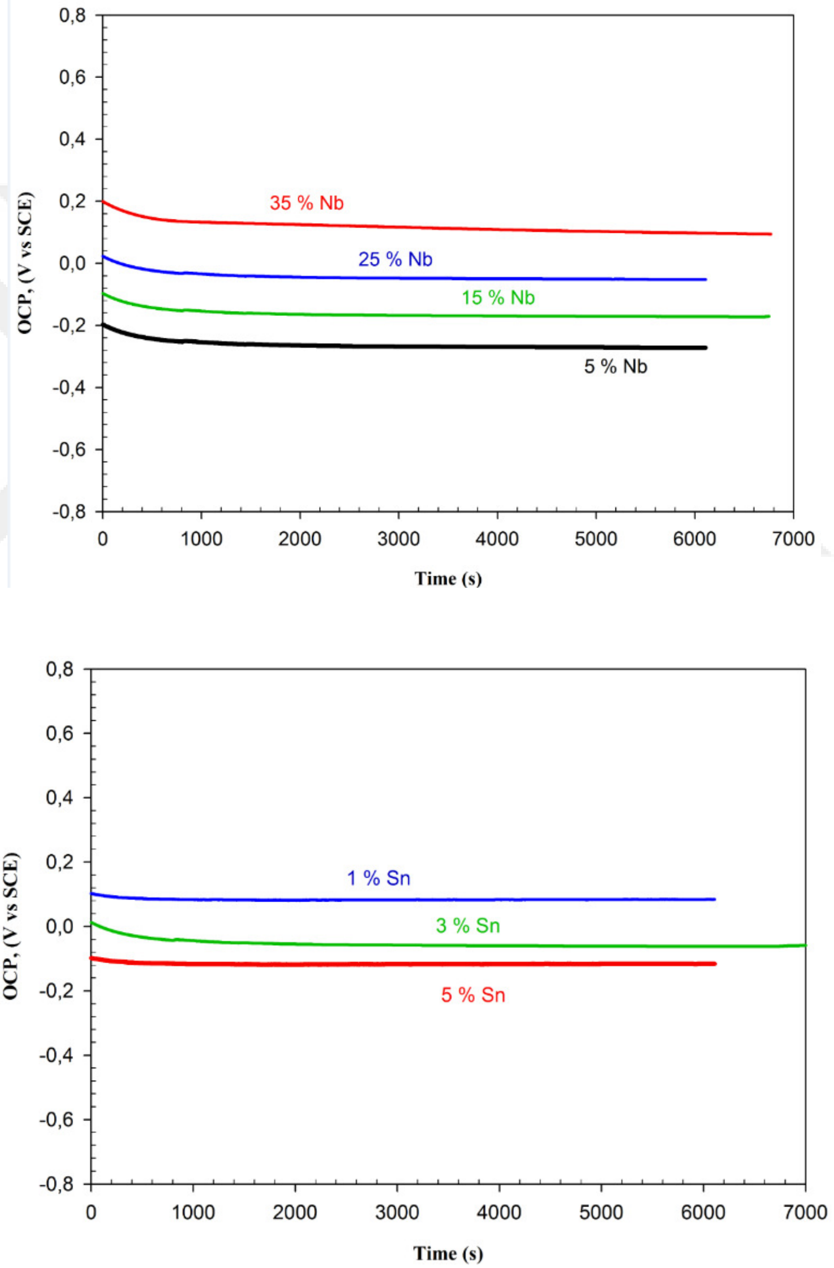


Figure 3.6: Variation of the OCP value with (a) Nb and (b) Sn contents of the alloy

Figure given below illustrates the effect of (a) Nb content of the alloy and (b) Sn content of the alloy on the Tafel curves. Tafel curves was used in order to evaluate the electrochemical corrosion behaviour of the specimens. Increasing Nb contents were increased the corrosion potential and decreased the corrosion current density (corrosion rate) of the specimens. On the other hand, Sn addition was slightly increased the corrosion rate of the sintered Ta based alloy.

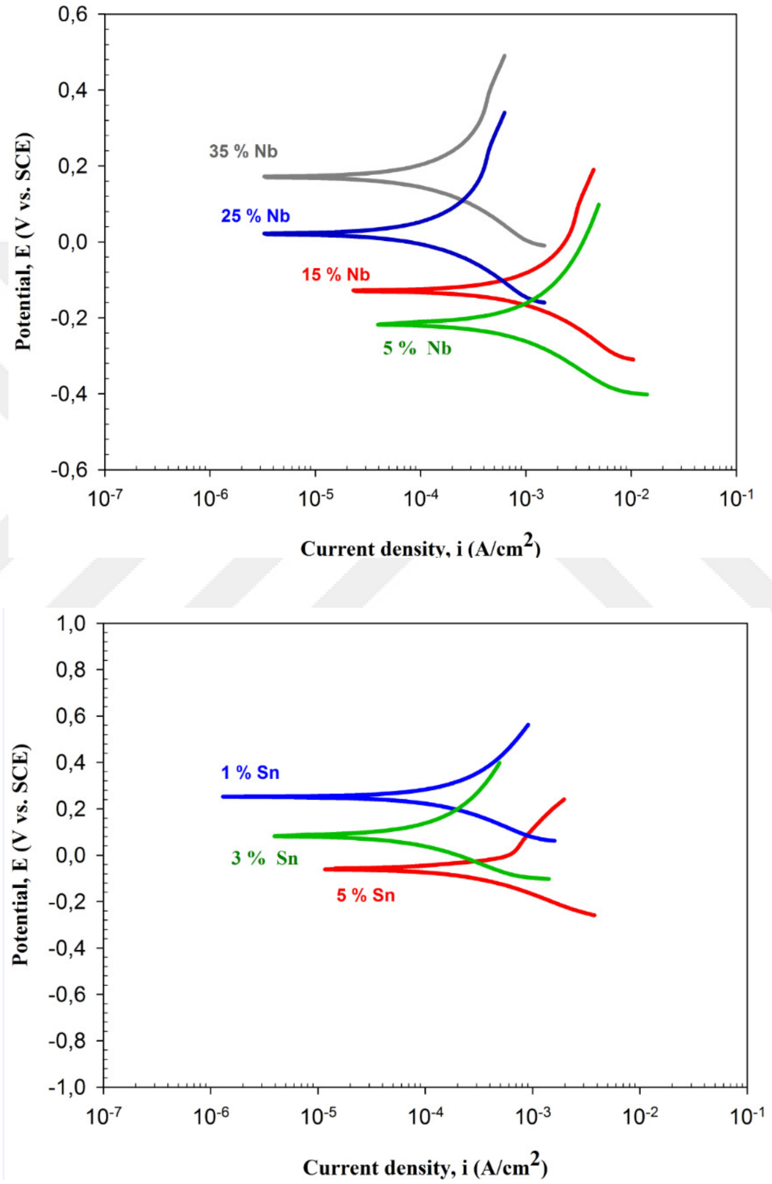


Figure 3.7: Effect of (a) Nb content and (b) Sn content on the Tafel curves

Figure given below shows the effect of Sn and Nb additions on the polarization resistance and corrosion rate. Sn addition was lowered the polarization resistance of samples. In general, Ta is very inert and resists to corrosion in the acidic solutions. Only highly acidic solutions containing fluoride ions can corrode the Ta. The inert nature of the Ta is very ideal for the biomedical implant applications. Inert nature and biocompatibility of the Ta is a consequence of the surface oxides. Ta has two types of surface oxide, Ta_2O_5 (more stable type) and TaO_2.

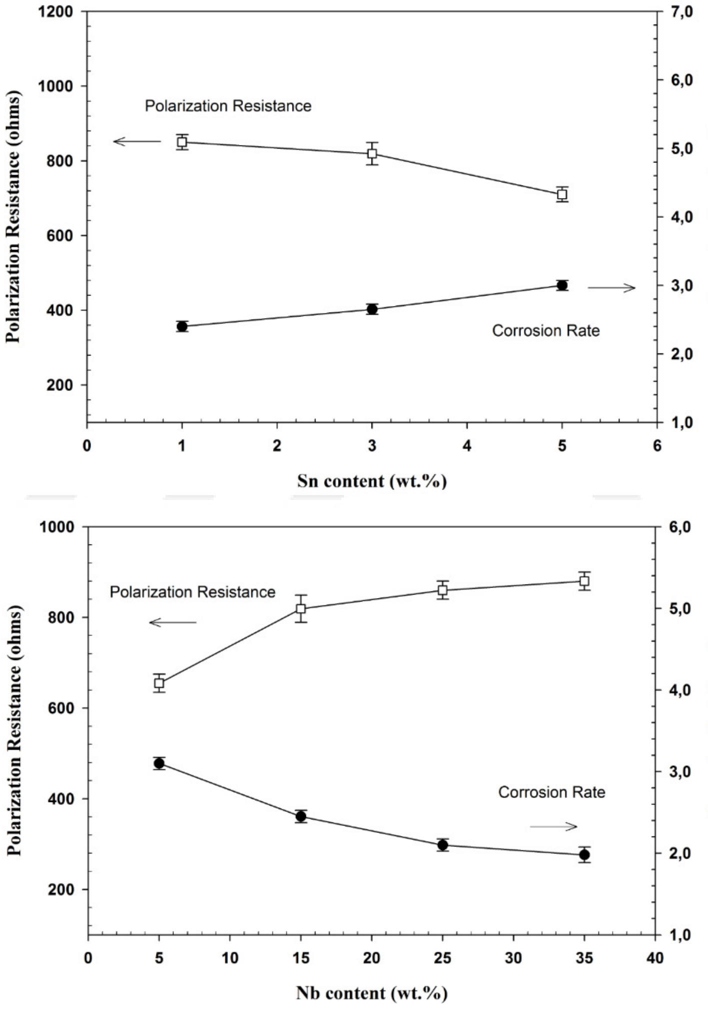


Figure 3.8: Effect of a) Sn and b) Nb on polarization resistance and corrosion rate

Figure given below illustrates the effect of static immersion time in SBF on the weight loss and Ta ion release of the Ta specimens. As seen from the figures, the weight change (loss) and metal (Ta) ion release values of the Ta alloy samples were increased with the time, as expected.

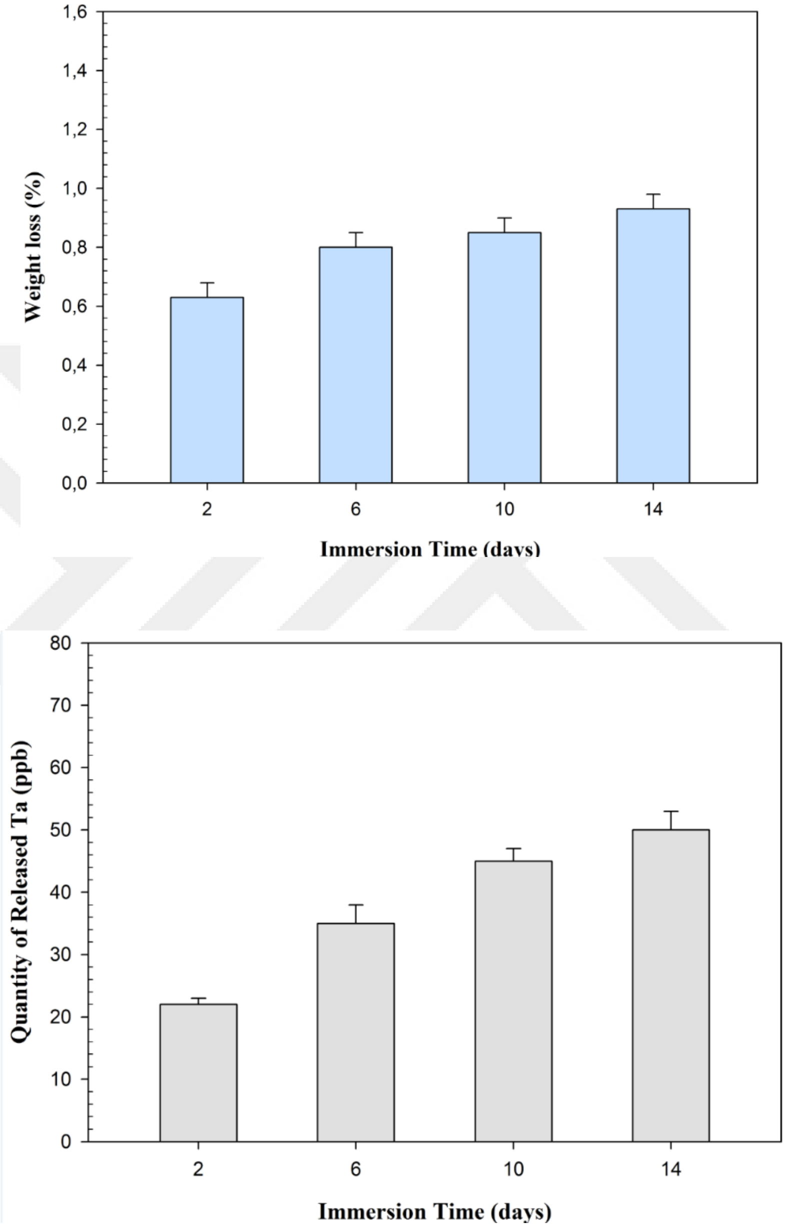


Figure 3.9: Effect of immersion time on (a) weight loss and (b) Ta ion release in SBF

Figure given below illustrates the effect of Nb contents of the Ta alloy on the (a) weight loss and (b) Ta ion release during the immersion tests in the SBF solution. As seen from the figures given below, increasing Nb content of the specimens decreased the weight loss and metal ion (Ta) release from the specimens.

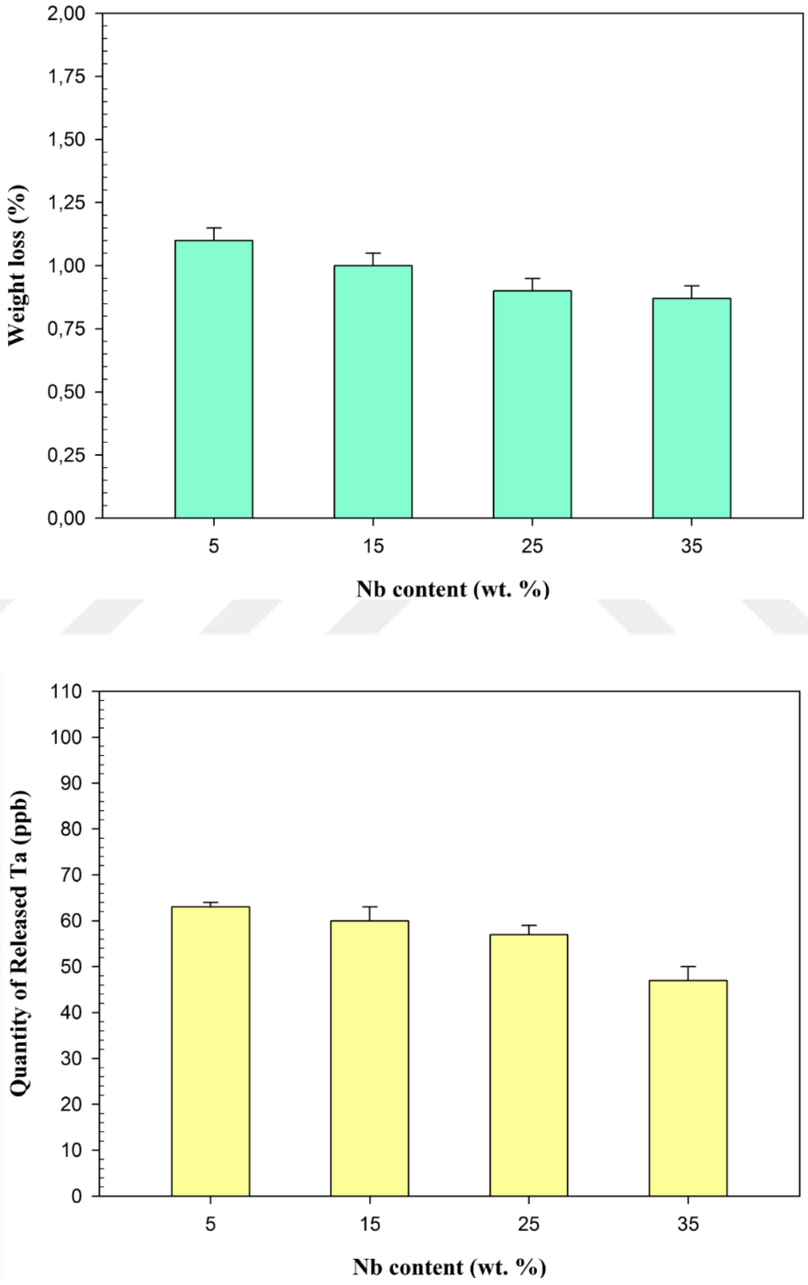


Figure 3.10: Effect of Nb content on (a) weight loss and (b) Ta ion release in SBF

Figure given below illustrates the effect of Sn contents of the Ta alloy on (a) weight loss and (b) Ta ion release in SBF solution. As seen from the figures given below, increasing Sn content of the specimens increased the weight loss and metal ion (Ta) release from the specimens.

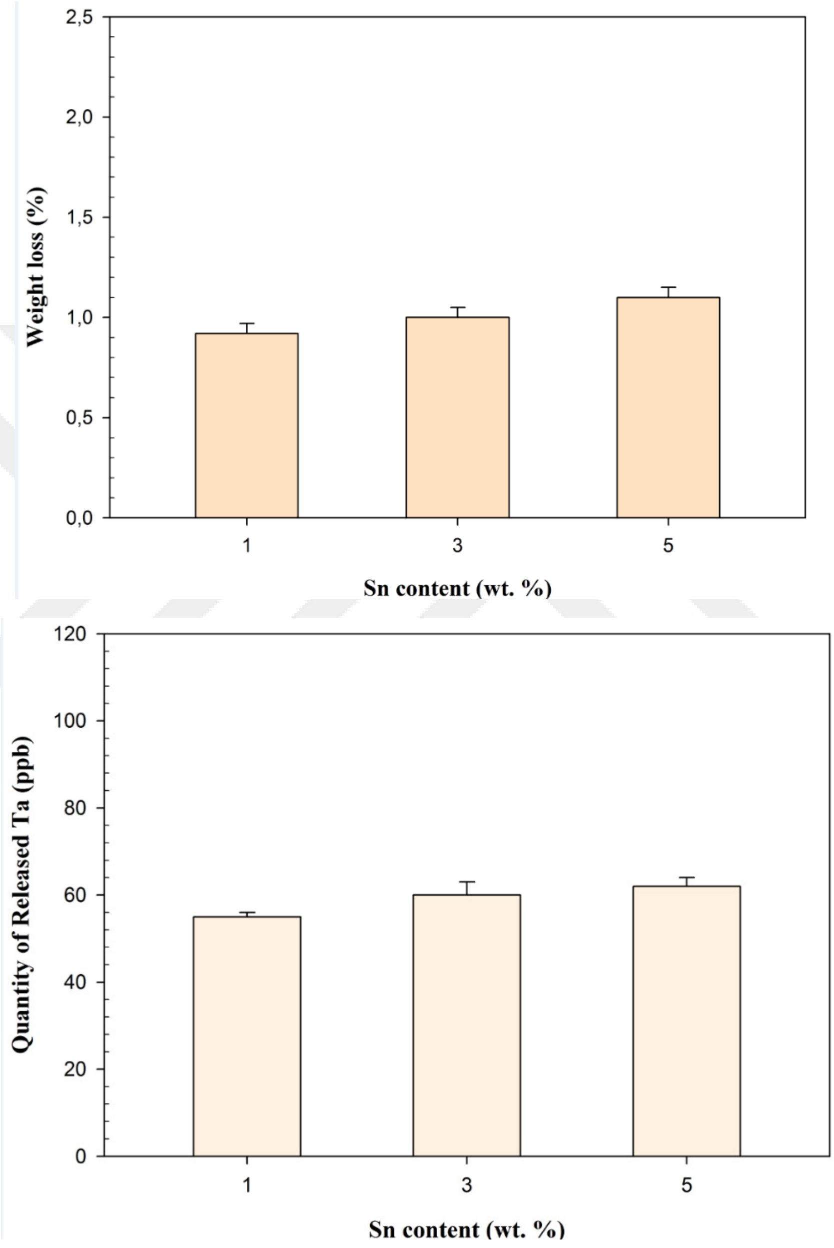
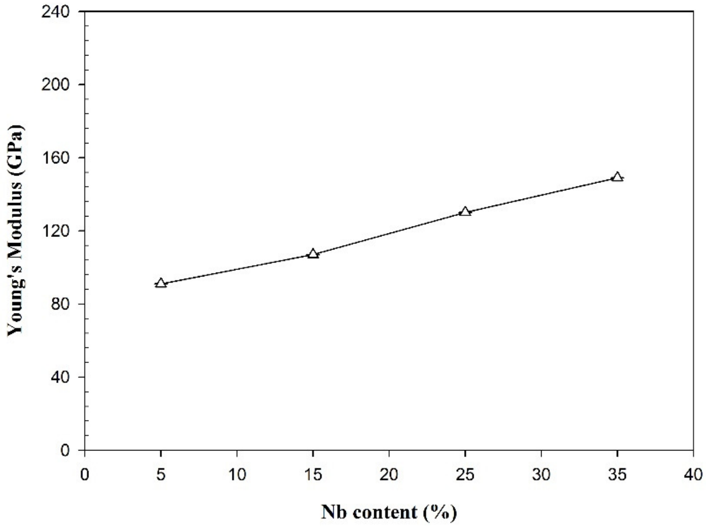


Figure 3.11: Effect of Sn content on (a) weight loss and (b) Ta ion release in SBF

Mechanical Properties of Ta Alloys

Figure given below illustrates the effects of Sn contents and Nb contents on the elastic modulus values of the sintered Ta alloy specimens. Elastic modulus values of the specimens were increased with increasing Nb contents and Sn contents. Increasing Nb contents increased the elastic modulus by solid solution strengthening. Increasing the Sn content enhances the densification of the Ta alloy that results increases in the elastic modulus.



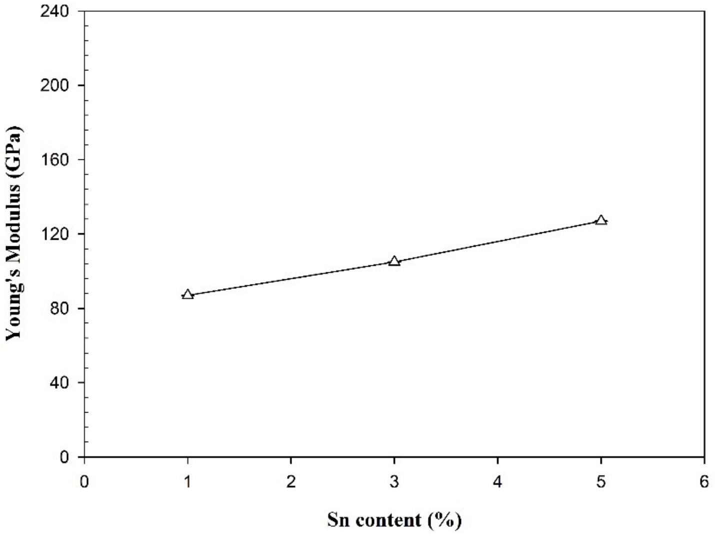
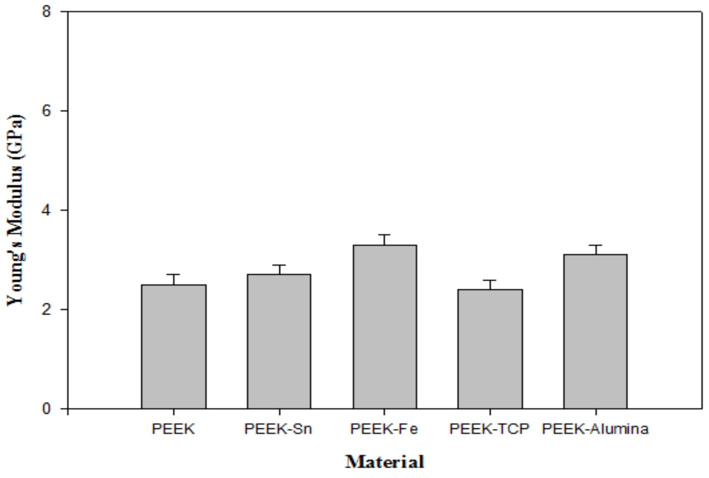


Figure 3.12: Effect of a) Nb and b) Sn contents on Young’s modulus

Mechanical Properties of PEEK Specimens

Figure given below exhibits the effect of powder addition (reinforcement) on the mechanical properties (elastic modulus and compressive tensile strength) of the PEEK matrix composite specimens. As seen from the Figure given below, compressive tensile strength and elastic modulus values of the PEEK matrix composite specimens were increased with powder addition, as expected. As seen from the Figure given below, the effect of Fe powder addition to the PEEK matrix was highest, while effect of tricalcium phosphate ($Ca_3(PO_4)_2$ or TCP) addition was slightly negative (decreased the mechanical properties).



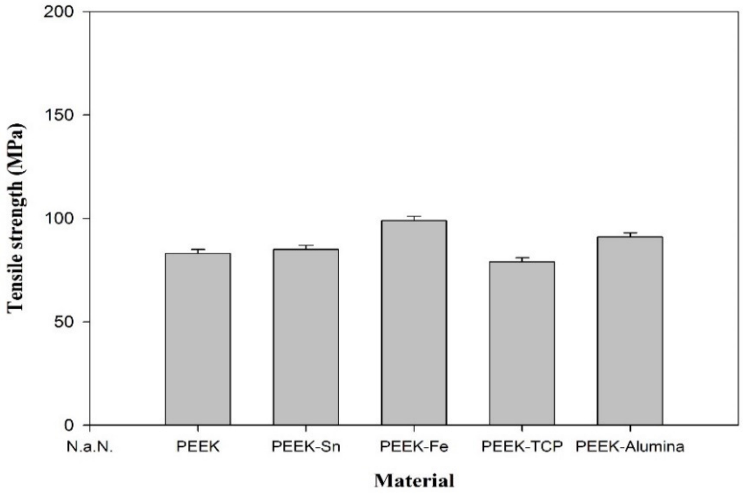


Figure 3.13: Effect of powder addition on a) Young's modulus b) strength of PEEK

Figure given below exhibits the effect of powder addition (reinforcement) on the hardness (Shore D) of the PEEK matrix composite specimens. As seen from the Figure given below, hardness values of the PEEK matrix composite specimens were increased with powder addition, as expected. In general, increasing hardness enhances the wear resistance of the materials, which is important in the hard tissue implant applications.

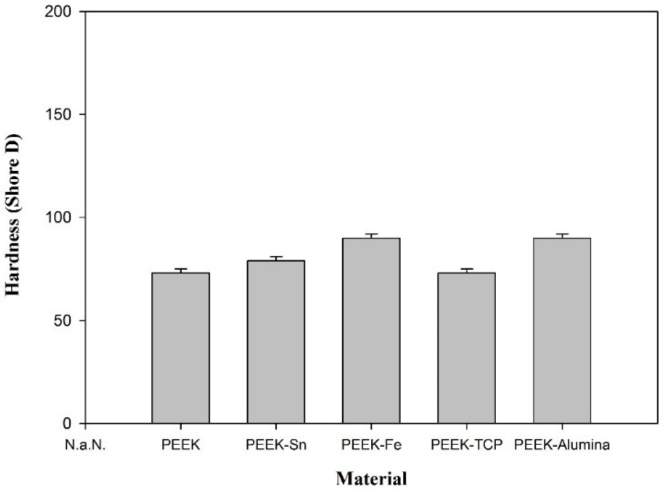


Figure 3.14: Effect of powder addition on the hardness of the PEEK samples

Figure given below exhibits the effect of Fe content on the hardness of the PEEK specimens. Hardness values of the specimens were increased with Fe content, as expected.

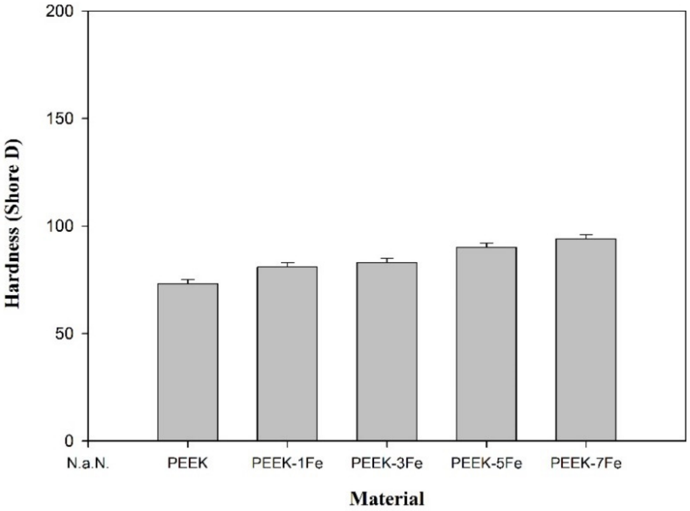


Figure 3.15: Effect of Fe content on the hardness of the PEEK samples

Figure given below exhibits the effect of TCP content on the hardness of the PEEK matrix composite specimens. Hardness values of the PEEK-TCP specimens were increased with increasing TCP content of the PEEK specimens. In general tricalcium phosphate ($Ca_3(PO_4)_2$) is a calcium salt of phosphoric acid. TCP is widely used in tissue engineering and for repairing the bone defects. TCP is biocompatible, bioactive and highly biodegradable. In the present study, TCP was included in order to enhance bioactivity.

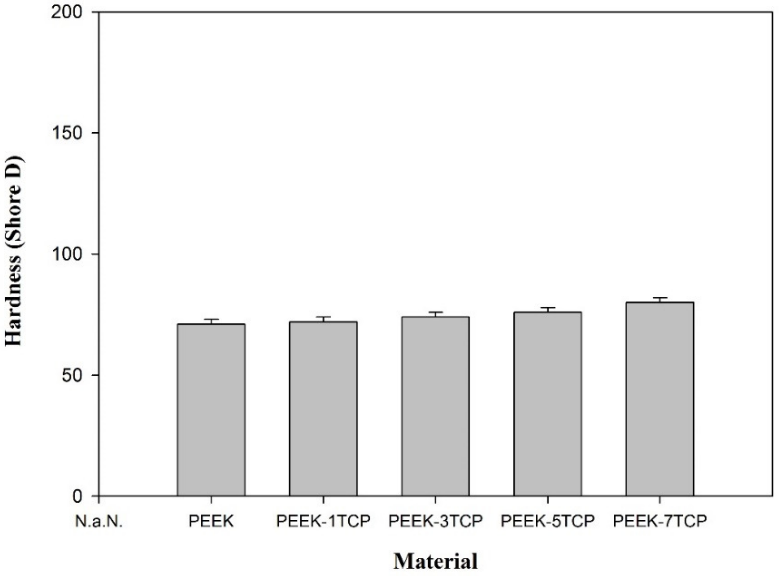


Figure 3.16: Effect of TCP content on the hardness of the PEEK samples

Contact Angle (Wettability)

In general, wettability is an important property for the biomaterials. In this study, wettability (contact angle) of the samples was studied by using optical tensiometer-contact angle meter (Attension Theta) by the sessile drop method. 5 mL water droplets were dropped on the samples at three different positions. Static contact angle was defined by fitting the Young-Laplace equation around the droplet. The mean water droplet contact angle for the PEEK and Ta-Nb-Sn alloys were about 80°. In general, as the contact angle is below 90°, the wettability of the Ta alloy is suitable for the biomedical implant applications, as expected. Figure given below shows the water droplets at the surface of the samples a) PEEK, and b) Ta alloy.

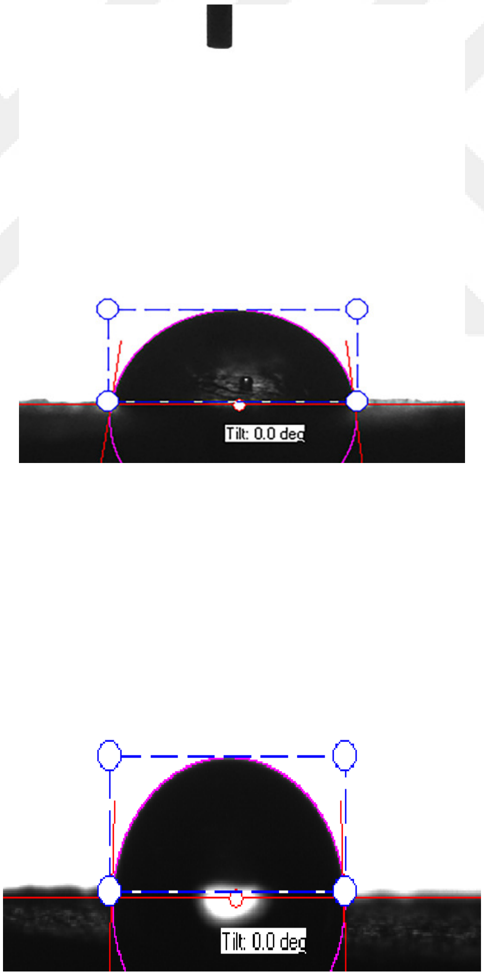


Figure 3.17: Photograph of the water droplets at the surface of the samples

Figure given below illustrates the Fourier Transform Infrared Spectroscopy (FT-IR) spectra of the sulfonated PEEK specimen (sPEEK). The peaks in the sulfonated PEEK specimen are due to symmetric O=S=O stretching and S=O stretching of the sulfonic functional group.

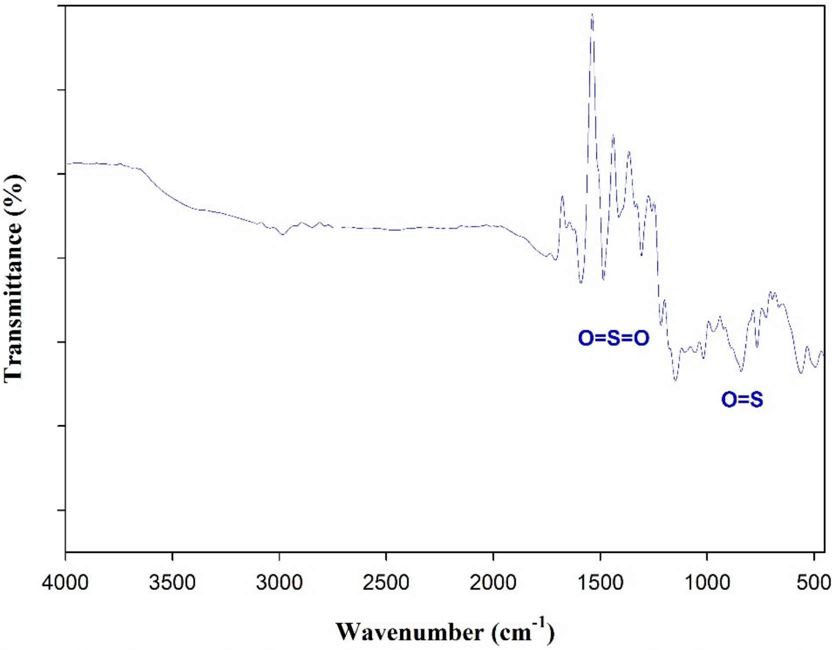


Figure 3.18: FTIR spectra of the sulfonated PEEK sample

4. DISCUSSION

In this thesis, manufacturing of the thermoplastic polyetheretherketone (PEEK) matrix composite specimens and metallic Ta alloy specimens were carried out by using the press-sinter (powder metallurgy) method. Polyetheretherketone (PEEK) matrix composite specimens and Ta based alloy specimens can be used as orthopaedical hard tissue implant material (spinal implant/intervertebral disc material).

In the PEEK based specimens:

- Fe powder was included in order to enhance the mechanical properties
- TCP powder was included in order to enhance the bioactivity
- Alumina powder was included in order to enhance the mechanical properties and wear resistance
- Sn powder was included in order to enhance the mechanical properties

In the Ta alloy specimens:

- Nb powder was included in order to enhance the mechanical properties and to reduce the price
- Sn powder was included in order to enhance the sinterability by liquid phase formation during sintering. In addition Sn was decreased the price of the alloy.
- Co powder was included in order to enhance the sinterability by liquid phase formation during sintering. In addition Co was decreased the price of the alloy.

Biomaterials may be natural or synthetic non-living materials and are employed in biomedical applications in order to support, enhance, or replace damaged organ or tissue. In general, the biomaterials are special gropu of engineering materials. The human spinal (vertebral) column, usually known as backbone, contains 33 vertebrae that are joined by intervertebral discs, ligaments, and facet joint capsules (connective tissue). Human spinal (vertebral) column (backbone) contains 33 vertebrae that are joined by fibrocartilage/bone-like intervertebral discs (IVD). In general, the vertebral column is important in the movement, protects the spinal cord, carry (supper) the weight of the body, and forms the axis of the body. In general, the IVD provides shock/impact absorption proeprties to the spine and human body. Intervertebral disc (IVD) supports external/internal loads, provides flexibility, and dissipates/absorb energy.

Polyetheretherketone (PEEK) is a thermoplastic polymer used in the engineering applications. PEEK is a semicrystalline thermoplastic with excellent mechanical and chemical resistance properties that are retained to high temperatures. Its elastic modulus is about 3.6 GPa and its tensile strength is about 100 MPa. Polyetheretherketone (PEEK) based specimens were produced by powder metallurgy method. PEEK based composite specimens were produced by fine PEEK powders. PEEK powders and additives (Fe, Sn, TCP, Alumina powders) were mixed and then compacted. Lastly the specimens were sintered.

Tantalum (Ta) is a rare, hard, easily fabricated, and dark blue-gray metal. Ta shows very high electrochemical corrosion resistance. In general, the Ta (tantalum) has high strength, ductility, corrosion resistance and biocompatibility. But, Ta has high price, high density and manufacturing of the Ta-based parts is difficult due to high melting temperature and affinity for oxygen. Nb and Sn additions to the Ta can reduce the melting temperature, the elastic modulus, and the price. In addition, artefacts and medical image distortions are very low in the Ta based implants. Ta based biomedical implants can be subdivide into 2 main groups: Ta based capacitors-implantable electronical devices and biomedical implants produced from or coated with Ta. Thin coating of Ta_2O_5 film on Ta is inert to human body fluids, that makes it ideal for biomedical implants. Biomedical Ta implants have been employed in medicine for 50 years without poblems.

In general, titanium cages/discs are "harder" than the bone and increase the chance of subsidence (cage sinks into vertebral endplates during inflammatory process of fusion). Titanium also produces MRI and CT artifact which make it difficult to visualize the fusion constrict. Ta and PEEK solved the subsidence problem and Ta and PEEK are imaging friendly. They are resistant to microbial adhesion and decrease the infection. But, PEEK does not integrate into the vertebral endplates (not bioactive).

In general, the powder metallurgy technique allows production of the Ta based alloys with very high melting temperatures. Production of the Ta alloy specimens with the casting methods would be very difficult due to their very high melting temperatures.

Powder metallurgy (P/M) can be described as technology of manufacturing metal components by using fine powders insted of conventional casting and ingot metallurgy. In general, a powder is a granular solid with particle size lower than 1 mm (usually about 30-100 μm).

In the experiments, the Ta based alloys were manufactured by using fine metal powders. Ta based green specimens were produced by the following steps: metal powder mixing step, Ta alloy preparation by mechanical alloying (ball mill), and pressing step. Then, the sintering process of the green specimens.

In the injection method, cylindrical product was manufactured by using injection-molding machine. Polymer based binder, which is important for mouldability/flowability, was consisted of 35-40 wt. % paraffin, 60-65 wt. % PE. The final mixture was included plastic binder (35-40 %) and metal powders (60-65 %). Injection temperature was 185 ºC. Polymers were removed by using heated hexane and heating. Lastly, the samples were sintered at 1300 ºC.

In addition, vertebral interbody lumbar cage (intervertebral disc) and lumbar vertebra prototypes were produced by additive manufacturing device (3-d printer).

The contact angle of the Ta based alloys was about 80°, which is suitable for the spinal implant (intervertebral disc) applications.

Young’s modulus values of the Ta alloy specimens were increased with increasing Nb contents and Sn contents. Increasing Nb contents increased the elastic modulus by solid solution strengthening. Increasing Sn enhances densification of the Ta alloy that results increases in the elastic modulus.

Effect of powder addition (reinforcement) on the hardness (Shore D) of the PEEK matrix composite specimens was investigated. Hardness values of the PEEK matrix composite specimens were increased with powder addition, as expected. In general, increasing hardness enhances the wear resistance of the materials, which is important in the hard tissue implant applications.

5. CONCLUSION AND RECOMMENDATIONS

In this thesis, manufacturing of the thermoplastic polyetheretherketone (PEEK) matrix composite specimens and metallic Ta alloy specimens were carried out by using the powder metallurgy method. PEEK matrix composite specimens and Ta based alloy specimens can be used as orthopaedical hard tissue implant material (spinal implant/intervertebral disc material).

The human spinal column contains 33 vertebrae that are joined by intervertebral discs, ligaments, and facet joint capsules. Human spinal column contains 33 vertebrae that are joined by fibrocartilage/bone-like intervertebral discs (IVD). In general, the IVD provides shock/impact absorption proeprties to the spine and human body. Intervertebral disc (IVD) supports external/internal loads, provides flexibility, and dissipates/absorb energy.

Polyetheretherketone (PEEK) is a thermoplastic polymer used in the engineering applications. PEEK is a semicrystalline thermoplastic with excellent mechanical and chemical resistance properties that are retained to high temperatures. Polyetheretherketone (PEEK) based specimens were produced by powder metallurgy method. PEEK based composite specimens were produced by fine PEEK powders. PEEK powders and additives (Fe, Sn, TCP, Alumina powders) were mixed and then compacted. Lastly the specimens were sintered.

In the PEEK specimens:

- Fe powder was included in order to enhance the mechanical properties
- TCP powder was included in order to enhance the bioactivity
- Alumina powder was included to enhance the mechanical properties and wear resistance
- Sn powder was included in order to enhance the mechanical properties

Tantalum (Ta) is a rare, hard, easily fabricated, and dark blue-gray metal. Ta shows very high electrochemical corrosion resistance. In general, the Ta (tantalum) has high strength, ductility, corrosion resistance and biocompatibility. But, Ta has high price, high density and manufacturing of the Ta-based parts is difficult due to high melting temperature and affinity for oxygen. Nb and Sn additions to the Ta can reduce the melting temperature, the elastic modulus, and the price. In addition, artefacts and medical image distortions are very low in the Ta based implants. Thin coating of Ta_2O_5 film on Ta is inert to human body fluids, that makes it ideal for biomedical implants. Biomedical Ta implants have been employed in medicine for 50 years without poblems.

In general, titanium cages/discs are "harder" then bone and increase the chance of subsidence (cage sinks into vertebral endplates during inflammatory process of fusion). Titanium also produces MRI and CT artifact which make it difficult to visualize the fusion constrict. Ta and PEEK solved the subsidence problem and Ta and PEEK are imaging friendly. They are resistant to microbial adhesion and decrease the infection. But, PEEK does not integrate into the vertebral endplates (not bioactive).

In general, the powder metallurgy technique allows production of the Ta based alloys with very high melting temperatures. Production of the Ta alloy specimens with the casting methods would be very difficult due to their very high melting temperatures.

In the experiments, the Ta based alloys were manufactured by using fine metal powders. Ta based green specimens were produced by the following steps: metal powder mixing step, Ta alloy preparation by mechanical alloying (ball mill), and pressing step. Then, the sintering process of the green specimens.

In the injection method, cylindrical product was manufactured by using injection-molding machine. Polymer based binder, which is important for mouldability/flowability, was consisted of 35-40 wt. % wax (paraffin), 60-65 wt. % polyethylene (PE). The final mixture was included plastic binder (35-40 %) and metal powders (60-65 %). Injection temperature of the process was 185 ºC. Polymers were removed by using heated hexane (for paraffin) and heating (for PE). Lastly, the samples were sintered at 1300 ºC.

In the Ta alloy specimens:

- Nb powder was included to enhance the mechanical properties and to reduce the price
- Sn powder was included in order to enhance the sinterability by liquid phase formation during sintering. In addition Sn was decreased the price of the alloy.
- Co powder was included in order to enhance the sinterability by liquid phase formation during sintering. In addition Co was decreased the price of the alloy.

The contact angle of the Ta based alloys was about 80°, which is suitable for the spinal implant (intervertebral disc) applications.

Increasing Nb contents increased the elastic modulus by solid solution strengthening. Raising Sn enhances densification of the Ta alloy that results increases in the elastic modulus.

Effect of powder addition (reinforcement) on the hardness (Shore D) of the PEEK matrix composite specimens was investigated. Hardness values of the PEEK matrix composite specimens were increased with powder addition, as expected. In general, increasing hardness enhances the wear resistance of the materials, which is important in the hard tissue implant applications.

As a result, Polyetheretherketone (PEEK) based polymer matrix composite specimens and Ta based alloys can be used in the orthopaedic implant (spinal implant (intervertebral disc)) applications. As the tantalum is radiopaque and nonmagnetic it is very suitable for the biomedical implant applications. In addition tantalum shows high biocompatibility and suitable mechanical properties.

REFERENCES

[1] Park J.B., Bronzino J.D.. 2007, Biomaterials, Principles and Applications, CRC Press, New York, USA.

[2] Pruitt L, 2011, Mechanics of Biomaterials, Fundamental Principles for Implant Design. Cambridge University Press, Cambridge, UK.

[3] Hendra Hermawan, 2012, Biodegradable Metals, From Concepts to Applications. Springer, London, UK

[4] Ratner, B. 2004, Biomaterials Science, An Introduction to Materials in Medicine, Elsevier.

[5] Huston Ronald, 2009, Principles of Biomechanics, Taylor-Francis Group, CRC Press.

[6] Winkelstein B.A., 2013, Orthopaedic Biomechanics, CRC Press.

[7]. Bayraktar, T.O., 2015, Çimentolu Proksimal Femoral Çivi Uygulamalarımızın Sonuçları, Tıpta Uzmanlık Tezi, Okmeydanı Sağlık Uygulama ve Araştırma Merkezi Ortopedi ve Travmatoloji Kliniği.

[8]. Aydın, A.T., 1999, Ön Çapraz Bağ Yaralanmasının Tedavisinde Endikasyonlar, Acta Orthop Traumatol Turc, (33), 385.

[9]. Ünal, Ö.K., 2012, Patellar veya Hamstring Tendon Otogrefiti Kullanılan ve Femura Tünel İçi Çivileme Sistemi ile Tespit Edilen Ön Çapraz Bağ Onarımlarının Tedavi Sonuçlarının Karşılaştırılması, Uzmanlık Tezi, Uludağ Üniversitesi Tıp Fakültesi Ortopedi ve Travmatoloji Anabilim Dalı.

[10]. Haglin J.M., Adam E.M., Joseph A.G., Stephen E.M., Botero-Hincapie J., Daniels A.H., 2016, Patient-Specific Orthopaedic Implants, orthopaedic Surgery, 8:417-424.

[11] Levine B., Valle C.J.D., Jacobs J.J., Applications of Porous Tantalum in Total Hip Arthroplasty. Journal of the American Academy of Orthopaedic Surgeons. 646-655.

[12] https://www.tanb.org/ (son ziyaret: 12.02.2021)

[13] Köck W., Paschen P., 1989, Tantalum, Processing, properties and Applications. 89 October, JOM, 33-39

[14]. Upadhyaya, G.S., 2002. *Powder Metallurgy Technology*, Cambridge International Science Publishing, England.

[15]. Zhao Y., Chang I., 2013, Advances in Powder Metallurgy, Processing, Properties and Applications. WP, Woodhead Publishing, Philadelphia, USA.

[16]. ASM Handbook, 1998, *Powder Metal Tehnologies and Applications, Volume 7,* ASM International.

[17] Kim Y., Lee D., Hwang J., Ryu H.J., Hong S.H., 2016, Fabrication and Characterization

of Powder Metallurgy Tantalum Components Prepared by High Compaction Pressure technique. Materials Characterization, 114, 225-233.

[18] Adamek G., Jakubowicz J., 2015, Tantalum Foam Made With Sucrose As A Space Holder, International Journal of Refractory Metals and Hard Materials, 53, 51-55.

[19] Ruperez E., Manero J.M., Riccardi K., Li Y., Aparico C., Gil F.J., 2015, Development of Tantalum Scaffold for Orthopedic Applications Produced by Space-Holder Method, Materials Design, 83, 112-119.

[20] Wang H., Yang J.L.H., Liu C., Ruan J., 2014, Fabrication, Characterization and In Vitro Biocompatibility Evaluation of Porous Ta-Nb Alloy for Bone Tissue Engineering, Materials Science and Engineering C, 40, 71-75.

[21] Kim Y., Kim E.P., Noh J.W., Lee S.H., Kwon Y.S., Oh I.S., 2015, Fabrication and Mechanical Properties of Powder Metallurgy Tantalum Prepared by Hot Isostatic Presing, International Journal of Refractory Metals and Hard Materials, 48, 211-216.

[22] Kurtz S.M., Devine J.N., 2007, PEEK Biomaterials in Trauma, Orthopedic and Spinal Implants, Biomaterials, 28(32), 4845-69.

CURRICULUM VITAE