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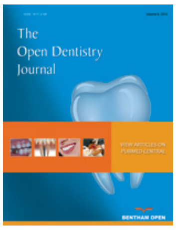

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SYSTEMATIC REVIEW

Osseointegration of Hafnium when Compared to Titanium - A Structured Review

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Abstract:

Aim:

This systematic review was conducted to analyse osseointegration of hafnium over conventional titanium.

Materials and Methods:

Search methodology was comprehended using PICO analysis and a comprehensive search was initiated in PubMed Central, Medline, Cochrane, Ovid, Science Direct, Copernicus and Google Scholar databases to identify the related literature. Randomised control trials, clinical studies, case control studies and animal studies were searched for osseointegration of hafnium coated titanium implants versus conventional titanium implants. Timeline was set to include all the manuscripts published till December 2018 in this review.

Clinical Significance:

Hafnium is a very promising surface coating intervention that can augment osseointegration in titanium implants. If research could be widened, including *in vivo* studies on hafnium as a metal for coating over dental implants or as a dental implant material itself to enhance better osseointegration, it could explore possibilities of this metal in the rehabilitation of both intra and extra oral defects and in medically compromised patients with poor quality of bone.

Results:

Out of the 25 articles obtained from the PICO based keyword search, 5 studies were excluded based on title and abstract. Out of the remaining 20 studies, 16 were excluded based on the inclusion and exclusion criteria of our interest and finally, 4 were included on the basis of core data.

Conclusion:

This systematic review observed hafnium metal exhibited superior osseointegration than titanium. Owing to its biocompatibility, hafnium could be an alternative to titanium, in the near future.

Keywords: Osseointegration, Hafnium, Conventional titanium, Bone implant contact, Titanium alloys, Tantalum.

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1. INTRODUCTION

The advent of tissue engineering provides a novel approach for the repair and reconstruction of bone defects [1 - 4]. An ideal implant material should have appropriate biocompatibility, corrosion resistance, elastic modulus, and favourable bone anchorage [5 - 12]. One of the most commonly used materials is titanium for its low elastic modulus, good corrosion resistance and biocompatibility. Hence it has become the most commonly used biomaterial for dental implants [13 - 15].

In various studies conducted to date, Tantalum has revealed superior properties fulfilling the criteria required for an implant [16 - 20]. Tantalum has been shown to be a promising material for excellent chemical stability, fluid body resistance, biological inertness and remarkable osteocon-

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ductivity [16 - 26]. Tantalum has higher elastic modulus than human bone tissue but it’s prone to stress shielding effect [27]. To overcome this, porous forms of tantalum have been explored [28 - 30]. However, the structure of porous tantalum renders it unsuitable for long-term use in the load-bearing structures [31]. Hence tantalum porous implants with titanium substructures have become more popular [18, 31, 32]. Similarly, plasma spraying tantalum over titanium is also reported [33].

In the periodic table by IUPAC 2016, tantalum belongs to period 6 (d block) of the periodic table [34]. Hafnium belongs to the same block as tantalum, in the periodic table, hence similar biological and chemical behaviour analogous to tantalum are expected and therefore, hafnium coatings and their biological applications have been vigorously researched upon. The metal was first identified by Dirck Coster and Georges de Hevesy in Copenhagen in 1923 and owed its name to ’Hafnia’, the Latin name for Copenhagen. Hafnium is always found in association with zirconium in mineral ores [35 - 37]. The main mineral where it is found in zircon, with a ratio Hafnium/Zirconium of about 2.5% [38]. Hafnium is a passive metal with various properties, such as high ductility, strength, resistance to corrosion and mechanical damage. Due to a number of interesting properties such as high ductility and strength, as well as resistance to corrosion and mechanical damage, it has attracted interest for a number of applications [37]. For instance, it is used as a control material for nuclear reactors and as an alloying element in some superalloys used in aircrafts engines [39, 40].

Hafnium has also been investigated as an alloying element in titanium alloys. Different proportions of Titanium-Hafnium binary alloys have been studied and reported in the literature [41]. These alloys have shown a low elastic modulus which is beneficial in order to reduce the stress shielding effect and to enhance bone growth. It has also been shown that cold work can be used to decrease the elastic modulus of this type of alloy, reaching values close to the elastic modulus of cortical bone [42].

In 1984, Marcel Pourbaix proposed hafnium as a metal to be considered for surgical implants due to the passive state of the metal. However, due to the lack of information about its toxicity to the human body at that time, it was discarded from the final list of metals to be theoretically considered. More recently, the properties of hafnium as an implant material have been investigated. Studies have shown that hafnium metal had both good biocompatibility and osteogenic potential.To date, the literature illustrating the behaviour of hafnium as a surface coating in biological environments has been scarce. Thus, further studies of hafnium coating under biological conditions are needed in order to determine the suitability of this material, as a surface coating for biomedical applications. The aim of the current review is to systematically analyse the scientific evidence on osseointegration of hafnium coatings in titanium implants.

2. MATERIALS AND METHODS

2.1. Structured Question

Is osseointegration in hafnium significantly greater than titanium?

PICO [Problem, Intervention, Comparison, and Outcomes]

P- Osseointegration

I- Hafnium

C- Conventional titanium

O- Bone implant contact

2.2. Data Collection and Analysis

The studies selected were based on the data extraction and analysis of quality and publication bias. The data collection form was customized. The outcome measure was bone implant contact.

2.3. Literature Search Protocol

2.3.1. Sources Used

For identification of studies included or considered for this systematic review, detailed search strategies were developed for the database searched. The search methodology applied was a combination of MESH terms and suitable key words. The key words employed in this search were broadly classified into four categories describing population, intervention, outcome and the type of study. Key words within each group were combined using Boolean operator [OR] and the searches of individual groups were combined using Boolean operator [AND] to retrieve articles electronically. The protocol is registered in PROSPERO (acknowledgements of receipt (166932)).

2.3.2. Searched Databases

The electronic databases included were: PubMed, Google Scholar, Medline, Ovid, Science Direct, Copernicus, Cochrane database of systematic reviews and no limitation regarding publication type and the publication date was set.

2.3.3. Search Terms

P- osseointegration, Osteoblast cell adhesion, Fibroblast cell adhesion, Bone cement, Tissue adhesion, Cell adhesion, Cellular wettability, Bone bonding, Bone adhesion, Bone formation, Bone integration, Bone remodelling, Bone fusion, Bone implant junction, Bone regeneration

I- zirconium mineral, zirconium minerals, Zircon, Hafnium isotope, Hafnium isotopes, hafnium coating, Hafnium coatings, Hafnium surface coating, Hafnium surface coatings, Nanoparticle hafnium coating, Bio inert coating, Bio inert coatings, Hafnium compounds, Hafnium compound

C-Titanium implant, Titanium implant, Titanium alloy, Titanium alloys

O-Removal torque, Bone implant contact

2.3.4. Article Eligibility Criteria

The inclusion criteria include articles reporting bone regeneration with hafnium and healing with no restrictions on age or gender or ethnicity, studies on bone regeneration with titanium and its alloys, animal studies, in-vitro studies, RCT,case-series. The exclusion criteria include studies using zirconium containing hafnium, studies with metals other than pure hafnium and titanium, review articles, studies with metal coatings other than hafnium and titanium, studies with metal alloys other than titanium and hafnium.

2.3.5. Article Selection

The title and abstract of the entries yielded from the initial electronic database searches were read. After this initial filter, the full-text versions of the studies that could be potentially included in this review were read and a final selection of articles was made after applying the eligibility criteria.

2.3.6. Structured Algorithm

Search [bone bonding OR osseointegration OR Osteoblast cell adhesion OR Fibroblast cell adhesion OR Bone cement OR Tissue adhesion OR Cell adhesion OR Cellular wettability OR Bone implant contact OR Bone adhesion OR Bone formation OR Bone integration OR Bone remodelling OR Bone fusion OR Bone implant junction OR Bone regeneration] AND [titanium implant OR Titanium implants OR Titanium alloy OR Titanium alloys] AND [hafnium OR zirconium mineral OR zirconium minerals OR Zircon OR Hafnium isotope OR hafnium isotopes OR hafnium coating OR hafnium coatings OR Hafnium surface coating OR Hafnium surface coatings OR Nanoparticle hafnium coating OR Nanoparticle hafnium coatings OR Bioinert coating OR Bioinert coatings OR Hafnium compound OR Hafnium compounds] AND [bone implant contact OR Removal torque OR Resonance frequency analysis].

3. RESULTS

Out of the 25 articles obtained from searching all databases, 5 studies were excluded based on title and abstract. Out of the remaining 20 studies, 16 were excluded based on the inclusion and exclusion criteria of our interest and 4 were included on the basis of core data (Table **1**). The 4 articles were reviewed and were consolidated as depicted in the flowchart below (Fig. **1**).

The treatment effects measured in these studies were bone-implant contact, percentage of new bone formation, cellular adhesion, and osteoblastic activity (Table **2**).

The data of the selected studies were extracted using standardized abstraction tables. Information extracted from each study included the following in one table as general characteristics of the study: 1) Title 2) Author and year 3) Study design 4) Duration 5) Intervention 6) Groups 7) Sample size 8) Types of statistical methods used 9) Outcome measures Table **3**.The outcome variables of the extracted data from the studies were interpreted in detail (Table **4**). The level of evidence, according to Oxford Centre for Evidence-Based Medicine 2011, was also tabulated (Table **5**).

4. DISCUSSION

This Systematic review reveals four articles evaluating osseointegration of hafnium over the gold standard metal titanium [43 - 45]. The studies show evidence that hafnium appears to have equivalent biocompatible properties as compared to Tantalum, Rhenium and other implant materials. However, the exclusions were not statistically significant and so larger studies with the stronger design are required to provide conclusive evidence on the exact effectiveness of Hafnium on osseointegration in human osseous tissues. A Meta-analysis could not be performed with the studies included, as the outcome parameters measuring the osseointegration were different in all the studies.

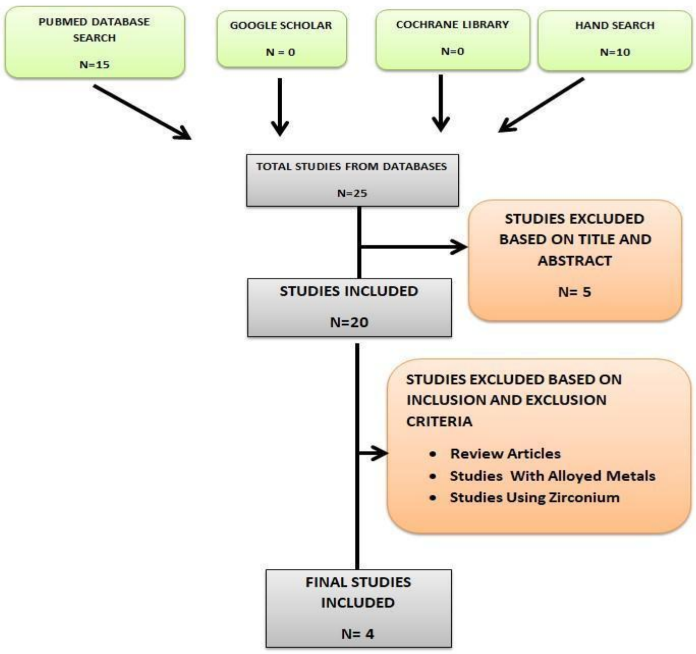

Fig. (1). Image presenting flowchart of the search methodology describing the total number of articles obtained, the ones that were excluded, inclusion of handpicked articles and finally the total number of articles that were retrieved for analysis.

The studies included in this review show significant bone gain with hafnium implants. All four included studies evaluated different outcome parameters making it difficult to consolidate the results over a single outcome measure. The outcome parameters used to study osseointegration in the studies included in this review were bone-implant contact, percentage of new bone formation, alkaline phosphatase levels in blood, cellular adhesion and cellular proliferation [26, 46 - 48].

Table 1. Table showing studies excluded from the systematic review on osseointegration of hafnium and reasons for their exclusion.

AUTHOR & YEAR	STUDY DESIGN	REASON FOR EXCLUSION
Akhtiamov *et al.* 2015	Animal study	Difference in the intervention group and outcome parameters
Herranz-Diez, *et al.* 2016	In-vitro study	Difference in intervention and outcome parameters
Jeong *et al.* 2009	In-vitro study	Difference in intervention group
Akhtiamov *et al.* 2015	Animal study	Difference in the intervention group
Wang *et al.* 2014	Literature review	Review article
Herranz-Diez *et al.* 2015	In-vitro study	Difference in intervention group and outcome parameters
Liu *et al.* 2017	Literature review	Review article
Sin *et al.* 2013	In-vitro study	Difference in outcome parameters
Qin *et al.* 2018	Literature review	Review article
Benic *et al.* 2017	Animal study	Intervention Group Contains Different Metal
Wang *et al.* 2016	Animal study	Difference in intervention group
AlFarraj AA *et al.* 2018	Animal study	Difference in intervention group
Cho Y *et al.* 2015	In-vitro study	Intervention Group Contains Different Metal
Kang HK *et al.* 2013	Animal study	Intervention Group And Comparison Group Contains Different Metal
Diefenbeck M *et al.* 2011	Animal study	Different Problem parameter
Shin D *et al.* 2011	Animal study	Intervention Group Contains Different Metal
Wen B *et al.* 2016	Animal study	Difference in intervention group
Wenz *et al.* 2008	Systematic Review	Review article
Kong YM *et al.* 2002	Animal study	Difference in intervention group
Dubruille JH *et al.* 1999	Animal study	Difference in intervention group
Li J *et al.*	Animal study	Difference in intervention group

Table 2. Table showing the types of outcome measures review related to osseointegration, used in studies included in this systematic review.

TYPES OF OUTCOME MEASURES
Bone Implant Contact
New Bone Formation
Alkaline Phosphatase Levels
Cellular Adhesion And Osteoblastic Activity

Table 3. Table showing the general information of all the included articles in this systematic review and the outcome measures used in those studies.

TITLE	AUTHOR YEAR	STUDY DESIGN	TIME PERIOD	INTERVEN TION	GROUPS	SAMPLE SIZE	STATISTICS	OUTCOME MEASURES
Tissue response to hafnium	Mohommadi S *et al.* 2001	Animal study	24 WEEKS	machined Hafnium non-threaded implants	Group 1=Hafnium implants in abdominal wall Group 2=Titanium implants in abdominal wall Group 3=Hafnium implants in Tibia Group 4=Titanium implants in tibia	N= 78 Group 1= 21 Group 2= 21 Group 3=18 Group 4= 18	Fishchers test, T test	1]tissue-implant interface were evaluated by light microscopy [morphometry] 2]Bone-implant contact and bone area within threads were evaluated in ground sections

(Table 3) contd.....

TITLE	AUTHOR YEAR	STUDY DESIGN	TIME PERIOD	INTERVENTION	GROUPS	SAMPLE SIZE	STATISTICS	OUTCOME MEASURES
Biocompatibility & osteogenesis of refractory metal implants, titanium, hafnium, niobium, tantalum & rhenium	H. Matsuno *et al.*. 2001	Animal study	4 WEEKS	refractory metal implants	titanium, hafnium, niobium, tantalum and rhenium wires	Not mentioned	one-factor ANOVA, Fisher's & Kruskal Wallis test.	Surface structure and roughness SOFT TISSUE: optical microscopy, X-ray scanning analytical Microscope & HARD TISSUE:optical microscopy, electron probe microanalyzer, reflected electrons, new bone formation
Effect of hafnium and titanium coated implants on several blood biochemical markers after osteosynthesis in rabbits	Yousef *et al.* 2014	Animal study	60 days	Medical steel 12X18H9T [C-0.2%; Si0.8%; Mn-2%; Ni-[8-9.5]%; S-0.02%; P-0.035%; Cr [17 - 19]%; Cu-0.3%; Fe-67%], coated with titanium and hafnium nitrides	Test group=medical steel coated with titanium and hafnium nitrides, with a diameter of 2 mm control group =non-coated medical steel with the same diameter was used	N =30 Individual group sample not mentioned	Student's t-test with a Bonferroni correction	1]alkaline phosphatase [ALP] [kinetic colorimetric method using ALP DGKC system test 2]level of calcium [photometric method] 3]phosphorus [spectrometric method 4]total protein, aspartate aminotransferase and alanine aminotransferase [AST, ALT], 5]the level of glucose [test system GLUC-PAP]
Cellular responses of osteoblast-like cells to 17 elemental metals	Zhang *et al.* 2016	In vitro study.	168 hours	Pure elemental metals	titanium[Ti], zirconium[Zr], hafnium[Hf], vanadium[V], niobium[Nb], tantalum[Ta], Chromium[Cr], molybdenum[Mo], manganese[Mn], iron[Fe], Ruthenium[Ru], cobalt[Co], nickel[Ni], copper[Cu], zinc [Zn], silicon[Si] & tin[Sn]	N=17	One-way ANOVA with post-hoc Turkey HSD	1]Protein adsorption 2]Cell adhesion 3]Cell proliferation 4]Cell morphology and actin cytoskeleton 5]Ion release 6]ALP activity and collagen content

Table 4. Table showing the details about the outcome variables, their statistical significance and conclusion of the studies included in this systematic review.

AUTHOR YEAR	OUTCOME MEASURE	MEAN ± SD	NUMBER OF CELLS	PERCENTAGE OF NEW BONE FORMATION	P VALUE	CONCLUSION
Mohommadi *et al.* 2001	Bone-implant contact	-	-	-	P>0.05	Hafnium and titanium were similar in inducing osteogenic properties.
H. Matsuno *et al.*. 2001	percentage of new bone formation	- -	-	After 2 weeks:10% for all the implants After 4 weeks: percentage had markedly increased for each metal	After 2 weeks p>0.05 After 4 weeks P<0.05	The results of animal implantation test of Titanium, Hafnium, Niobium, Tantalum and Rhenium in both soft and hard tissue of rats showed that they have good biocompatibility and osteogenesis.

(Table 4) contd.....

AUTHOR YEAR	OUTCOME MEASURE	MEAN ± SD	NUMBER OF CELLS	PERCENTAGE OF NEW BONE FORMATION	P VALUE	CONCLUSION
Yousef *et al.* 2014	Alkaline phosphatase	5th day post-operative Test[coated]=166.16±18.56 Control[uncoated]=146.36±18.63 60th day post-operative Test[coated] =136.27±15.87 Control[uncoated]=142.41±21.62	-	-	5th day P<0.05 60th day p>0.05	Nano-technologically coated implants with a bio inert combination of titanium and hafnium nitrides for the purpose of prevention of the possible complication, such as individual intolerance of patient to the implants. There was no difference between the groups after 60 days.
Zhang *et al.* 2016	Cellular adhesion &cellular proliferation	-	No. of cells adhered on Ti & Hf discs increased gradually upto 4h & no. of SaOS2 cells significantly higher than control group after 168h	-	P<0.05	Good cell proliferation was observed on discs of group 1 metals comprising Titanium, Hafnium etc.

Table 5. Table showing the CEBM level of evidence of included studies.

STUDY	STUDY DESIGN	CEBM LEVEL OF EVIDENCE
Mohommadi S *et al.* 2001	Animal study	Level 5
H. Matsuno *et al.*. 2001	Animal study	Level 5
Yousef *et al.* 2014	Animal study	Level 5
Zhang *et al.* 2016	In vitro study.	Level 5

It is well established that measuring bone implant contact is the standard gold technique for the measurement of osseointegration in animal models [49 - 51]. Similarly, measuring the cell proliferation of osteoblastic cell lines is the gold standard technique for *in vitro* studies [52 - 54]. Hence it is justifiable to give more weightage to the studies measuring the gold standard outcome measures [55 - 59]. Apart from the above-mentioned parameters, the biochemical marker alkaline phosphatase is also considered an adjunct aid to prove significant osseointegration [52, 60, 61].The current evidence in the available literature shows that hafnium also promotes superior osteogenic cell proliferation when compared to titanium. The limitations of this review are the *in vitro* nature of the studies included with level 5 evidence, *in vivo* intervention in animal models and the absence of randomized control human trials with both titanium and hafnium coatings over the implant surfaces in varying clinical situations [58, 62]. Hence the inference needs to be interpreted prudently [63 - 67].

CONCLUSION

Based on this systematic review, hafnium is a very promising surface coating intervention that can augment osseointegration in titanium implants. However, this needs to be validated through rigorous long-term clinical trials. Owing to its biocompatibility and osseointegrative properties, hafnium could be an alternative to titanium, in the near future.

CLINICAL SIGNIFICANCE

Hafnium is a very promising surface coating intervention that can augment osseointegration in titanium implants. If research could be widened including *in vivo* studies on hafnium as a metal for coating over dental implants or as a dental implant material itself to enhance better osseointegration, it could explore possibilities of this metal in rehabilitation of both intra and extra oral defects and in medically compromised patients with poor quality of bone.

CONSENT FOR PUBLICATION

Not applicable.

STANDARDS FOR REPORTING

PRISMA guidelines and methodology were followed.

FUNDING

None.

CONFLICT OF INTEREST

The author declare no conflict of interest, financial or otherwise.

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REFERENCES

[1] Fishero BA, Kohli N, Das A, Christophel JJ, Cui Q. Current concepts of bone tissue engineering for craniofacial bone defect repair. Craniomaxillofac Trauma Reconstr 2015; 8(01): 023-30. [http://dx.doi.org/10.1055/s-0034-1393724]

[2] Chanchareonsook N, Junker R, Jongpaiboonkit L, Jansen JA. Tissue-engineered mandibular bone reconstruction for continuity defects: a systematic approach to the literature. Tissue Eng Part B Rev 2014; 20(2): 147-62. [http://dx.doi.org/10.1089/ten.teb.2013.0131] [PMID: 23865639]

[3] Juneja SC, Schwarz EM, O'Keefe RJ, Awad HA. Cellular and molecular factors in flexor tendon repair and adhesions: a histological and gene expression analysis. Connect Tissue Res 2013; 54(3): 218-26. [http://dx.doi.org/10.3109/03008207.2013.787418] [PMID: 23586515]

[4] Nakahara T, Nakamura T, Kobayashi E, *et al.* Novel approach to regeneration of periodontal tissues based on in situ tissue engineering: effects of controlled release of basic fibroblast growth factor from a sandwich membrane. Tissue Eng 2003; 9(1): 153-62. [http://dx.doi.org/10.1089/107632703762687636] [PMID: 12625964]

[5] Benzel EC. Biomechanics of spine stabilization. Rolling Meadows 2001; pp. 437-40.

[6] Smith DC. Surface characterization of implant materials, Biological implications. The bone-biomaterials interface 1991; 3-18.

[7] Solar RJ. Corrosion resistance of titanium surgical implant alloys: a review. Corrosion and degradation of implant materials 1979 Oct ASTM International. 1979; In: ASTM International.;

[8] Greene ND. Corrosion of surgical implant alloys: A few basic ideas. *Corrosion and degradation of implant materials* second symposium. 1985; In: ASTM International.;

[9] Syrett BC, Wing SS. An electrochemical investigation of fretting corrosion of surgical implant materials. Corrosion 1978; 34(11): 378-86. [http://dx.doi.org/10.5006/0010-9312-34.11.378]

[10] Song XP, You L, Zhang B, Song A. Design of low elastic modulus Ti–Nb–Zr alloys for implant materials. Mater Technol 2012; 27(1): 55-7. [http://dx.doi.org/10.1179/175355511X13240279340921]

[11] Gabet Y, Kohavi D, Voide R, Mueller TL, Müller R, Bab I. Endosseous implant anchorage is critically dependent on mechanostructural determinants of peri-implant bone trabeculae. J Bone Miner Res 2010; 25(3): 575-83. [http://dx.doi.org/10.1359/jbmr.090808] [PMID: 19653813]

[12] Sakka S, Coulthard P. Bone quality: a reality for the process of osseointegration. Implant Dent 2009; 18(6): 480-5. [http://dx.doi.org/10.1097/ID.0b013e3181bb840d] [PMID: 20009601]

[13] Baumgarten HS. Why titanium in dental applications?. Titanium in Medical and Dental Applications 2018; pp. 495-504.

[14] Graft W, Rostoker W. The measurement of elastic modulus of titanium alloys. Symposium on Titanium. [http://dx.doi.org/10.1520/STP44151S]

[15] Saini M, Singh Y, Arora P, Arora V, Jain K. Implant biomaterials: A comprehensive review. World J Clin Cases 2015; 3(1): 52-7. [http://dx.doi.org/10.12998/wjcc.v3.i1.52] [PMID: 25610850]

[16] Wegrzyn J, Kaufman KR, Hanssen AD, Lewallen DG. Performance of porous tantalum vs. titanium cup in total hip arthroplasty: randomized trial with minimum 10-year follow-up. J Arthroplasty 2015; 30(6): 1008-13. [http://dx.doi.org/10.1016/j.arth.2015.01.013] [PMID: 25765132]

[17] Lu MM, Wu PS, Guo XJ, Yin LL, Cao HL, Zou D. Osteoinductive effects of tantalum and titanium on bone mesenchymal stromal cells and bone formation in ovariectomized rats. Eur Rev Med Pharmacol Sci 2018; 22(21): 7087-104. [PMID: 30468450]

[18] Bencharit S, Byrd WC, Altarawneh S, *et al.* Development and applications of porous tantalum trabecular metal-enhanced titanium dental implants. Clin Implant Dent Relat Res 2014; 16(6): 817-26. [http://dx.doi.org/10.1111/cid.12059] [PMID: 23527899]

[19] Zhou X, Hu X, Lin Y. Coating of sandblasted and acid-etched dental implants with tantalum using vacuum plasma spraying. Implant Dent 2018; 27(2): 202-8. [http://dx.doi.org/10.1097/ID.0000000000000727] [PMID: 29394178]

[20] Lambert JB. Tantalum and tantalum compounds. Kirk-Othmer Encyclopedia of Chemical Technology 2000 Dec 4;

[21] Tripp TB, Eckert J. Tantalum and tantalum compounds. Kirk-Othmer Encyclopedia of Chemical Technology 2000 Dec 4;

[22] Miyaza T, Kim HM, Kokubo T, Ohtsuki C, Kato H, Nakamura T. Mechanism of bonelike apatite formation on bioactive tantalum metal in a simulated body fluid. Biomaterials 2002; 23(3): 827-32. [http://dx.doi.org/10.1016/S0142-9612(01)00188-0] [PMID: 11771702]

[23] Gurappa I. Characterization of different materials for corrosion resistance under simulated body fluid conditions. Mater Charact 2002; 49(1): 73-9. [http://dx.doi.org/10.1016/S1044-5803(02)00320-0]

[24] Black J. Biological performance of tantalum. Clin Mater 1994; 16(3): 167-73. [http://dx.doi.org/10.1016/0267-6605(94)90113-9] [PMID: 10172264]

[25] Takematsu E, Noguchi K, Kuroda K, Ikoma T, Niinomi M, Matsushita N. In vivo osteoconductivity of surface modified Ti-29Nb-13Ta-4.6Zr alloy with low dissolution of toxic trace elements. PLoS One 2018; 13(1): e0189967. [1]. [http://dx.doi.org/10.1371/journal.pone.0189967] [PMID: 29342150]

[26] Matsuno H, Yokoyama A, Watari F, Uo M, Kawasaki T. Biocompatibility and osteogenesis of refractory metal implants, titanium, hafnium, niobium, tantalum and rhenium. Biomaterials 2001; 22(11): 1253-62. [http://dx.doi.org/10.1016/S0142-9612(00)00275-1] [PMID: 11336297]

[27] Dai K. Rational utilization of the stress shielding effect of implants. Biomech and Biomat in Ortho 2004; 208-15.

[28] Paganias CG, Tsakotos GA, Koutsostathis SD, Macheras GA. Osseous integration in porous tantalum implants. Indian J Orthop 2012; 46(5): 505-13. [http://dx.doi.org/10.4103/0019-5413.101032] [PMID: 23162141]

[29] de Arriba CC, Alobera Gracia MA, Coelho PG, *et al.* Osseoincorporation of porous tantalum trabecular-structured metal: a histologic and histomorphometric study in humans. Int J Periodontics Restorative Dent 2018; 38(6): 879-85. [http://dx.doi.org/10.11607/prd.3004] [PMID: 29513775]

[30] Lee JW, Wen HB, Gubbi P, Romanos GE. New bone formation and trabecular bone microarchitecture of highly porous tantalum compared to titanium implant threads: A pilot canine study. Clin Oral Implants Res 2018; 29(2): 164-74. [http://dx.doi.org/10.1111/clr.13074] [PMID: 28971532]

[31] Krishna BV, Bose S, Bandyopadhyay A. Fabrication and characterization of porous Ti6Al4V parts for biomedical applications using electron beam melting process. J Acta Biomater 2007; 3: 997-1006. [http://dx.doi.org/10.1016/j.actbio.2007.03.008]

[32] Medlin DJ, Scrafton J, Shetty R. Metallurgical attachment of a porous tantalum foam to a titanium substrate for orthopedic applications. Titanium, Niobium, Zirconium, and Tantalum for Medical and Surgical Applications 2006 Jan ASTM International 2006.

[33] Vetrivendan E, Jayaraj J, Ningshen S, Mallika C, Mudali UK. Argon shrouded plasma spraying of tantalum over titanium for corrosion protection in fluorinated nitric acid media. J of Therml Spray Technol 2018; 27(3): 512-23. [http://dx.doi.org/10.1007/s11666-017-0678-7]

[34] Damhus T, Hartshorn RM, Hutton AT. Nomenclature of inorganic chemistry: IUPAC recommendations 2005. Chem Int 2005.

[35] Coster D, Hevesy G. On celtium and hafnium. Nature 1923; 111(2788): 462-3. [http://dx.doi.org/10.1038/111462a0]

[36] Mukherji AK. Analytical Chemistry of Zirconium and Hafnium: International Series of Monographs in Analytical Chemistry. Elsevier 2013.

[37] Cheng KL. Determination of zirconium and hafnium with xylenol orange and methylthymol blue. Anal Chim Acta 1963; 28: 41-53. [http://dx.doi.org/10.1016/S0003-2670(00)87194-9]

[38] Predel B. Hf-Zr [Hafnium-Zirconium]. In: Ga-Gd–Hf-Zr. Springer, Berlin, Heidelberg. 1996; pp. 1-4.

[39] Risovany VD, Prokhorov VI, Ostrovsky ZE, Pimenov VV, Zakharov AV, Muraleva EM. Structure and properties of hafnium after a 9-year operation in the RBT-6 research reactor. J Nucl Mater 2010; 402(2-3): 157-61. [http://dx.doi.org/10.1016/j.jnucmat.2010.05.011]

[40] Ruane TF, Storm ML. Epithermal hafnium parameters for the calculation of control rod worth in thermal reactors. Nucl Sci Eng 1959; 6(2): 119-27. [http://dx.doi.org/10.13182/NSE59-A25641]

[41] Liu X, Chen S, Tsoi JKH, Matinlinna JP. Binary titanium alloys as dental implant materials-a review. Regen Biomater 2017; 4(5): 315-23.

[http://dx.doi.org/10.1093/rb/rbx027] [PMID: 29026646]
[42] Venugopalan S, Ariga P, Aggarwal P, Viswanath A. Magnetically retained silicone facial prosthesis. Niger J Clin Pract 2014; 17(2): 260-4. [http://dx.doi.org/10.4103/1119-3077.127575] [PMID: 24553044]
[43] Ganapathy D, Sathyamoorthy A, Ranganathan H, Murthykumar K. Effect of resin bonded luting agents influencing marginal discrepancy in all ceramic complete veneer crowns. J Clin Diagn Res 2016; 10(12): ZC67-70. [http://dx.doi.org/10.7860/JCDR/2016/21447.9028] [PMID: 28209008]
[44] Duraisamy R, Krishnan CS, Ramasubramanian H, Sampathkumar J, Mariappan S, Navarasampatti Sivaprakasam A. Compatibility of nonoriginal abutments with implants: Evaluation of microgap at the implant-abutment interface, with original and nonoriginal abutments. Implant Dent 2019; 28(3): 289-95. [http://dx.doi.org/10.1097/ID.0000000000000885] [PMID: 31124826]
[45] Ozan S, Lin J, Li Y, Wen C. New Ti-Ta-Zr-Nb alloys with ultrahigh strength for potential orthopedic implant applications. J Mech Behav Biomed Mater 2017; 75: 119-27. [http://dx.doi.org/10.1016/j.jmbbm.2017.07.011] [PMID: 28711024]
[46] Mohammadi S, Esposito M, Cucu M, Ericson LE, Thomsen P. Tissue response to hafnium. J Mater Sci Mater Med 2001; 12(7): 603-11. [http://dx.doi.org/10.1023/A:1011237610299] [PMID: 15348253]
[47] Yousef A, Akhtiamov I, Shakirova F, Zubairova L, Gatina E, Aliev E. Changes of blood composition in rabbits before and after osteosynthesis utilizing coated and non-coated metal implants. International Journal of Biomedical and Healthcare Science 2014; 4(1): 21-7.
[48] Zhang D, Wong CS, Wen C, Li Y. Cellular responses of osteoblast-like cells to 17 elemental metals. J Biomed Mater Res A 2017; 105(1): 148-58. [http://dx.doi.org/10.1002/jbm.a.35895] [PMID: 27601355]
[49] Huwais S, Meyer EG. A novel osseous densification approach in implant osteotomy preparation to increase biomechanical primary stability, bone mineral density, and bone-to-implant contact. Int J Oral Maxillofac Implants 2017; 32(1): 27-36. [1]. [http://dx.doi.org/10.11607/jomi.4817] [PMID: 27741329]
[50] Trisi P, Lazzara R, Rao W, Rebaudi A. Bone-implant contact and bone quality: evaluation of expected and actual bone contact on machined and osseotite implant surfaces. Int J Periodontics Restorative Dent 2002; 22(6): 535-45. [6]. [PMID: 12516825]
[51] Lian ZQ, Guan H, Loo YC. Optimum degree of bone-implant contact in bone remodelling induced by dental implant. Procedia Eng 2011; 14: 2972-9. [http://dx.doi.org/10.1016/j.proeng.2011.07.374]
[52] Yang F, Dong WJ, He FM, Wang XX, Zhao SF, Yang GL. Osteoblast response to porous titanium surfaces coated with zinc-substituted hydroxyapatite. Oral Surg Oral Med Oral Pathol Oral Radiol 2012; 113(3): 313-8. [http://dx.doi.org/10.1016/j.tripleo.2011.02.049] [PMID: 22676822]
[53] Martins A, Pinho ED, Faria S, *et al.* Surface modification of electrospun polycaprolactone nanofiber meshes by plasma treatment to enhance biological performance. Small 2009; 5(10): 1195-206. [http://dx.doi.org/10.1002/smll.200801648] [PMID: 19242938]
[54] Selvan SR, Ganapathy D. Efficacy of fifth generation cephalosporins against methicillin-resistant *Staphylococcus aureus*-A review. Research Journal of Pharmacy and Technology 2016; 9(10): 1815-8. [http://dx.doi.org/10.5958/0974-360X.2016.00369.3]
[55] Subasree S, Murthykumar K. Effect of aloe vera in oral health-A review. Res J of Phar and Tech 2016; 9(5): 609-12. [http://dx.doi.org/10.5958/0974-360X.2016.00116.5]
[56] Vijayalakshmi B, Ganapathy D. Medical management of cellulitis. Res J of Phar and Tech 2016; 9(11): 2067-70. [http://dx.doi.org/10.5958/0974-360X.2016.00422.4]
[57] Jyothi S, Robin PK, Ganapathy D. Periodontal health status of three different groups wearing temporary partial denture. Res J of Phar and Tech 2017; 10(12): 4339-42. [http://dx.doi.org/10.5958/0974-360X.2017.00795.8]
[58] Kannan A. Effect of coated surfaces influencing screw loosening in implants: A systematic review and meta-analysis. WORLD 2017; 8(6): 496-502.
[59] Cui H, Wang Y, Cui L, *et al.* In vitro studies on regulation of osteogenic activities by electrical stimulus on biodegradable electroactive polyelectrolyte multilayers. Biomacromolecules 2014; 15(8): 3146-57. [http://dx.doi.org/10.1021/bm5007695] [PMID: 24995801]
[60] Parfitt AM, Simon LS, Villanueva AR, Krane SM. Procollagen type I carboxy-terminal extension peptide in serum as a marker of collagen biosynthesis in bone. Correlation with Iliac bone formation rates and comparison with total alkaline phosphatase. J Bone Miner Res 1987; 2(5): 427-36. [http://dx.doi.org/10.1002/jbmr.5650020510] [PMID: 3455625]
[61] Lee A, Langford CR, Rodriguez-Lorenzo LM, Thissen H, Cameron NR. Bioceramic nanocomposite thiol-acrylate polyHIPE scaffolds for enhanced osteoblastic cell culture in 3D. Biomater Sci 2017; 5(10): 2035-47. [http://dx.doi.org/10.1039/C7BM00292K] [PMID: 28726876]
[62] Ashok V, Nallaswamy D, Benazir Begum S, Nesappan T. Lip bumper prosthesis for an acromegaly patient: a clinical report. J Indian Prosthodont Soc 2014; 14(1)(Suppl. 1): 279-82. [http://dx.doi.org/10.1007/s13191-013-0339-6] [PMID: 26199531]
[63] Basha FY, Ganapathy D, Venugopalan S. Oral hygiene status among pregnant women. Res J of Phar and Tech 2018; 11(7): 3099-102. [http://dx.doi.org/10.5958/0974-360X.2018.00569.3]
[64] Ajay R, Suma K, Ali SA, *et al.* Effect of surface modifications on the retention of cement-retained implant crowns under fatigue loads: An *in vitro* study. J Pharm Bioallied Sci 2017; 9(Suppl. 1): S154-60. [http://dx.doi.org/10.4103/jpbs.JPBS_146_17] [PMID: 29284956]
[65] Ashok V, Suvitha S. Awareness of all ceramic restoration in rural population. Res J of Phar and Tech 2016; 9(10): 1691-3. [http://dx.doi.org/10.5958/0974-360X.2016.00340.1]
[66] Jain AR, Nallaswamy D, Ariga P, Ganapathy DM. Determination of correlation of width of maxillary anterior teeth using extraoral and intraoral factors in Indian population: A systematic review. World J Dent 2018; 9: 68-75. [http://dx.doi.org/10.5005/jp-journals-10015-1509]
[67] Rajaraman V, Dhanraj M, Jain AR. Dental implant biomaterials–Newer metals and their alloys. Drug Invention Today 2018; 10(6): 986-9.