A comparative evaluation of ion release from different commercially-available orthodontic mini-implants – an in-vitro study

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Background: Titanium alloy mini-implants have become popular in recent times and have been extensively used and studied. Although corrosion resistance of orthodontic materials has always been of concern, this property has been the least explored. The present study aimed to assess the composition, surface characterisation and corrosion resistance of five commercially available mini-implants by assaying ion release in artificial saliva.

Methods: Ten mini-implants each from five companies were obtained: Group 1 – AbsoAnchor (Dentos Inc, South Korea); Group 2 – Microimplant Anchorage System (MIA, Biomaterials Korea); Group 3 – The Orthodontic Mini Anchorage System (TOMAS, Dentaurum, Germany); Group 4 – mini-implants (Denticon, Maharashtra, India); Group 5 – orthodontic mini-implants (J.J.Orthodontics, Kerala, India). One mini-implant from each group was subjected to characterisation and surface microstructure analysis using Energy Dispersive Atomic Spectrometry (EDAX) and Scanning Electron Microscope (SEM), respectively. Ten mini-implants were immersed for 30 days in Fusayama-Meyer artificial saliva solution and the release of titanium, aluminium and vanadium ions was detected with Inductively Coupled Plasma - Optical Emission Spectrometry (ICP-OES). The Kruskal-Wallis test was used for multi-variate analysis. In order to determine the significant differences between the groups on independent samples, the Mann-Whitney U test (bi-variate analysis) was applied.

Results and conclusion: All groups showed machining defects but surface pitting after immersion was mostly evident in Group 4. Although the composition of all the implants was comparable, there was a statistically significant difference in the Ti, Al and V release between Group 4 – the group with maximum release – and Group 2, the group with least release.

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Introduction

Anchorage is defined as the resistance to unwanted tooth movement.1 Anchorage control in all three planes of space often determines the success of orthodontic treatment and most clinicians recognise this challenge during treatment planning. The introduction of micro-implants by Kanomi,2 in 1997, has revolutionised the science of anchorage by serving as a source of absolute stability. Mini-implants, in contrast to the prostodontic implants, are temporarily fixed to bone and have been used to accomplish various tooth movements in orthodontics.3,8

Based on the metals used for their manufacture, mini-implants can be classified as commercially pure titanium (cpTi) or a Ti alloy (containing titanium, aluminium and vanadium).9 Although the cpTi implants were widely used due to their excellent biocompatibility and corrosion resistance, they lacked adequate fracture resistance since the thin structure of the mini-implant was unable to bear high orthodontic loads. Therefore, commercially pure titanium was alloyed with aluminium and vanadium to offer greater strength and fatigue resistance.10 However, the corrosion resistance of the Ti alloy has been reported to be less than for pure titanium.11
Corrosion in the oral cavity is caused by ion release, and this has been extensively evaluated with reference to orthodontic brackets,12 fixed appliances13 and other appliances.14 Reported studies have predominantly shown that nickel and chromium release was significant.

Several animal studies have evaluated the corrosive properties and ion release from Ti alloy mini-implants.11,15 A significant amount of titanium and vanadium was released within four weeks of insertion in rabbits, although the concentration of the ions did not reach toxic levels.15 However, contrary studies have indicated that mini-implants could induce a cytotoxic reaction16,17 and published case reports have shown that dental implants could also have allergenic properties.18-20

It has been documented that aluminium and vanadium ions have toxic effects. Lin et al. showed that Al2O3 nanoparticles have a dose-dependent cytotoxicity in human bronchoalveolar carcinoma-derived cells at 5–25 mg/L doses.21 Aluminium has also been associated with an increased risk of developing Alzheimer’s disease.22 In patients with chronic renal failure, aluminium has been detected at the osteoid-calcified matrix interface in bone, which results in an interference with mineralisation leading to osteomalacia.23

Vanadium is considered to be a more toxic element compared with aluminium mainly due to a subtle difference in the level of toxic dose.15 Vanadium ions bind to the transport proteins, ferritin and transferritin, and affect their distribution throughout the body.24 Vanadium has also been reported to exhibit a dose-related effect on the inhibition of the mitotic index leading to chromosomal aberrations.25 A potential cytotoxic effect of vanadium on macrophages has been reported and an oral exposure of less than 0.01 mg vanadium/kg/day (Minimal Risk Level) has been documented to have health effects in humans.27

Only one human study has evaluated ion release from mini-implants in orthodontic patients.28 However, studies on retrieved mini-implants have shown localised pitting and crevice corrosion, principally at the sites of manufacturing defects.29,30 Therefore, the purpose of the present in-vitro study was to assay the release of titanium, aluminium and vanadium ions from five different commercially-available mini-implant systems. In addition, a subjective analysis of corrosion and pitting using an SEM was conducted.

**Materials and methods**

A total of 50 mini-implants were obtained for the study. All had the following characteristics: small head, conical thread, length of 6.0 mm and diameter of 1.5 mm. Ten mini-implants were obtained from five different companies and were grouped as follows: (Figure 1)

- Group 1 – AbsoAnchor (Dentos Inc, South Korea)
- Group 2 – Microimplant Anchorage System (MIA, Biomaterials, Korea)
- Group 3 – The Orthodontic Mini Anchorage System (TOMAS, Dentaaurum, Germany)
- Group 4 – Mini-implants (Denticon, Maharashtra, India)
- Group 5 – Orthodontic mini-implants (J.J.Orthodontics, Kerala, India)

One mini-implant from each group was subjected to characterisation (detection of elemental percentage composition) using Energy Dispersive Atomic Spectrometry (EDAX). Surface microstructure...
was analysed with the help of a Scanning Electron Microscope (SEM) in three different regions of each mini-implant. The characterisation and surface microstructure analysis were conducted using the FEI Quanta FEG 200 - High Resolution Scanning Electron Microscope, equipped with an Energy Dispersive Spectrometer, operated in a high vacuum (HV) mode in the Department of Nanotechnology, SRM University, Kattankulathur. The secondary and back-scattered images of the samples subjected to Scanning Electron Microscopy were visualised and recorded with the SEM operated at high vacuum (5.1 x 10^-6 Pa), 30 kV accelerating voltage and 105 µA specimen current. The samples were viewed at various magnifications ranging from 50× to 300×.

Following SEM and EDAX analysis, each of the five groups was further segregated into sub-groups ‘a’, ‘b’, ‘c’ and ‘d’ containing one, two, three, and four mini-implants respectively. The mini-implant subjected to SEM and EDAX constituted subgroup ‘a’ of each major group.

The sub-groups were immersed in 200 ml calibrated glass beakers containing Fusayama-Meyer artificial saliva solution. This solution was prepared in the Department of Biochemistry, Sri Ramachandra University, Chennai. The composition of this electrolyte solution was potassium chloride (KCl) (0.4 g/l), sodium chloride (NaCl) (0.4 g/l), calcium chloride (CaCl₂) (0.6 g/l), anhydrous monobasic sodium phosphate (NaH₂PO₄) (0.690 g/l) and urea (1 g/l). Each of the above ingredients was weighed (Sartorius scale) and incorporated into distilled water and stirred. The pH of the solution was adjusted to 5.8 using a pH meter (ELICO, Andhra Pradesh, India) and the temperature was maintained at 37°C in an incubator (ILE Co, Tamil Nadu, India) for the entire study period of 30 days. 200 ml of the artificial saliva solution with no mini-implants served as a control solution.

After 30 days, 50 ml of the solution from all of the sub-groups was collected to detect the release of titanium, aluminium and vanadium ions with the help of Inductively Coupled Plasma - Optical Emission Spectrometry (ICP-OES) at the Bureau Veritas Consumer Products Services Pvt. Ltd, Guindy, Chennai. Table I presents the operational parameters of ICP-OES. The values were recorded in mg/l.

Subsequent to the ion release detection, the mini-implant from sub-group ‘a’ of all the groups was thoroughly dried and resubmitted for SEM analysis.

### Statistical analysis

The collected data were entered into the SPSS software (version 17.0) to generate the mean, standard deviation and other statistical parameters necessary for descriptive statistical analysis. The Kruskal-Wallis test was used for the multi-variate analysis. In order to determine the significant differences between the groups on independent samples, the Mann-Whitney U test (bi-variate analysis) was applied. The probability value of $p \leq 0.05$ was considered as significant.

### Results

#### Characterisation of mini-implants using EDAX

The atomic percentage composition of the various mini-implants is depicted by the Energy Dispersion (EDS) spectra (Figure 2). The percentage values are tabulated for comparison (Table II).

| Group | Ti content (at. %) | C content (at. %) | Al content (at. %) | V content (at. %) |
|-------|-------------------|------------------|-------------------|------------------|
| 1     | 71.54             | 18.97            | 4.50              | 2.43             |
| 2     | 80.44             | 15.36            | 3.74              | 2.35             |
| 3     | 88.57             | 9.87             | 1.56              | 1.86             |
| 4     | 90.34             | 9.03             | 0.67              | 0.91             |
| 5     | 91.90             | 8.23             | 0.56              | 0.74             |

| Power (kW) | Plasma gas flow rate (L/min) | Auxiliary gas flow rate (L/min) | Nebuliser gas flow rate (L/min) | Replicate time (s) | Stab time (s) | View | Wavelength (nm) |
|------------|-----------------------------|---------------------------------|---------------------------------|-------------------|---------------|------|-----------------|
| 1.20       | 15.0                        | 1.50                            | 0.75                            | 1000              | 15            | Axial| 396.152 (Al)    |
|            |                             |                                 |                                 |                   |               |      | 336.122 (Ti)    |
|            |                             |                                 |                                 |                   |               |      | 311.837 (V)    |
respectively (10.07 at. % and 8.28 at. %).

**SEM analysis**

The results of the SEM analysis showed that, even before immersion, there were microscopic surface irregularities and machining defects in the form of dents and scratches in all the mini-implant groups. These characteristics were most evident in Group
Figure 3. Back scattered SEM images of Group 1 mini-implants.

Figure 4. Back scattered SEM images of Group 2 mini-implants.

Figure 5. Back scattered SEM images of Group 3 mini-implants.

Figure 6. Back scattered SEM images of Group 4 mini-implants.
followed by Group 1. Blunt edges were noted at certain regions in the head and threads of the mini-implants from Group 4 and Group 1. The former also had scratches along the conical thread and at the screw tip. Despite the surface defects, all the mini-implants had a glossy architecture.

The SEM images obtained after the immersion revealed generalised loss of gloss and surface finish with a consequentially dull appearance in all tested groups. Group 4 and Group 1 exhibited signs of corrosion in the form of crevices or pitting. This was seen principally at the sites of machining defects. The surface pits were also observed at the screw tips of mini-implants from Group 5. All the groups had integuments that were scattered over the surface of the mini-implants (Figures 3–7).

**Ion release**

Table III denotes the descriptive statistics of the mean values of Ti, Al and V release of the groups. Group 4 had the highest amount of Ti, Al, and V release when compared to other groups. Aluminium was released from all groups, with Group 3 showing the lowest release. Titanium was found to be below detectable

|       | N  | Mean   | Std. deviation |
|-------|----|--------|----------------|
| Titanium |    |        |                |
| Group 1 | 10 | 0.100000 | 0.0027080 |
| Group 2 | 10 | 0.000000 | 0.0000000 |
| Group 3 | 10 | 0.000000 | 0.0000000 |
| Group 4 | 10 | 0.306500 | 0.0815015 |
| Group 5 | 10 | 0.088000 | 0.0139284 |
| Total  | 50 | 0.098900 | 0.1186141 |
| Aluminium |    |        |                |
| Group 1 | 10 | 0.330800 | 0.0022509 |
| Group 2 | 10 | 0.151000 | 0.0208487 |
| Group 3 | 10 | 0.084500 | 0.0222224 |
| Group 4 | 10 | 0.619700 | 0.1607151 |
| Group 5 | 10 | 0.240100 | 0.0455130 |
| Total  | 50 | 0.285220 | 0.2021540 |
| Vanadium |    |        |                |
| Group 1 | 10 | 0.000000 | 0.0000000 |
| Group 2 | 10 | 0.000000 | 0.0000000 |
| Group 3 | 10 | 0.000000 | 0.0000000 |
| Group 4 | 10 | 0.165900 | 0.0349681 |
| Group 5 | 10 | 0.066000 | 0.0152096 |
| Total  | 50 | 0.046380 | 0.0676606 |
limits (BDL) in Groups 2 and 3. Vanadium showed below detectable limits (BDL) in Groups 1, 2 and 3. Table IV indicates that the multiple comparisons of means of Ti, Al and V release between the five groups were statistically highly significant at p values of < 0.01. The Mann-Whitney test for the bi-variate comparison of Ti release revealed that the differences in the mean values between Group 4 and all the other groups were statistically highly significant. The bi-variate analysis of Al release between groups showed statistically significant difference levels in the mean values of Al release between all the groups. The bi-variate analysis for V showed that Group 4 and Group 5 had statistically highly significant differences when compared with all the other groups. These results are tabulated in Table V.

**Discussion**

Commercially pure titanium offers high corrosion resistance due to the formation of a dense passive film of a rutile-type of Ti oxide (TiO2) of tetragonal structure.\(^3\)\(^1\) This layer is formed on the implant surface by a natural passivation process wherein titanium reacts instantaneously with oxygen from the bio-environment.\(^3\)\(^2\) In contradistinction, the Ti alloy is manufactured as a fusion of α and β phases in order

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**Table IV.** Kruskal-Wallis test for multiple comparison of means of Ti, Al and V ion release among the groups.

| Ion        | Group | N | Mean rank |
|------------|-------|---|-----------|
| Titanium   | Group 1 | 10 | 33.50     |
|            | Group 2 | 10 | 10.50     |
|            | Group 3 | 10 | 10.50     |
|            | Group 4 | 10 | 45.50     |
|            | Group 5 | 10 | 27.50     |
|            | Total   | 50 |           |
| Aluminium  | Group 1 | 10 | 34.65     |
|            | Group 2 | 10 | 15.50     |
|            | Group 3 | 10 | 5.50      |
|            | Group 4 | 10 | 45.50     |
|            | Group 5 | 10 | 26.35     |
|            | Total   | 50 |           |
| Vanadium   | Group 1 | 10 | 15.50     |
|            | Group 2 | 10 | 15.50     |
|            | Group 3 | 10 | 15.50     |
|            | Group 4 | 10 | 45.50     |
|            | Group 5 | 10 | 35.50     |
|            | Total   | 50 |           |

**Table V.** Mann-Whitney U test for bivariate comparison of Ti, Al and V release between groups.

| Ion        | Statistics | Group 1, 2 | Group 1, 3 | Group 1, 4 | Group 1, 5 | Group 2, 3 | Group 2, 4 | Group 2, 5 | Group 3, 4 | Group 3, 5 | Group 4, 5 |
|------------|------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
| Ti         | Mann – Whitney U | 0.000 | 0.000 | 0.000 | 20.000 | 50.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
|            | Exact Sig. (1-tailed) | 0.000 | 0.000 | 0.023 | 1 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Al         | Mann – Whitney U | 0.000 | 0.000 | 0.000 | 8.500 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
|            | Exact Sig. (1-tailed) | 0.000 | 0.000 | 0.001 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| V          | Mann – Whitney U | 50.000 | 50.000 | 0.000 | 0.000 | 50.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
|            | Exact Sig. (1-tailed) | 1.000 | 1.000 | 0.000 | 0.000 | 1.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
to combine their positive properties.\textsuperscript{10} The $\alpha$ phase offers mechanical resilience and tenacity but ductility is low. The $\beta$ phase offers formability and fatigue resistance at extreme temperatures but at the cost of being susceptible to atmospheric contamination.\textsuperscript{10} The surface oxide film of this alloy is composed of an amorphous Ti oxide along with small amounts of alumina, hydroxyl groups and bound water.\textsuperscript{15} Aluminium and vanadium are added to stabilise the $\alpha$ and $\beta$ phases of titanium. This, however, destabilises the surface oxide film, making it more susceptible to corrosion.\textsuperscript{33} In aqueous, dynamic conditions such as the oral environment, there is a slow continuous cycle of partial dissolution and re-precipitation of the surface oxide film. The presence of chloride ions, amino acids and proteins, and low pH, provides a conducive oral environment leading to the partial dissolution or disruption of the surface oxide film.\textsuperscript{34} In addition, wear and tear of the mini-implants in the oral cavity may also cause breakdown of the surface oxide film.\textsuperscript{33}

The release of Ti, V and Al are concerning because vanadium, when absorbed in high doses, brings about acute and chronic toxic effects.\textsuperscript{25} It also interferes with transport proteins which affects their distribution and accumulation in the body.\textsuperscript{25} The high affinity towards tissues has a high risk of the ions accumulating in tissues such as liver, kidney, and lungs.\textsuperscript{15}

Shi and Dalal in 1990\textsuperscript{35} detected vanadate (IV) formation in the NADPH-dependent reduction of vanadate (V) by lipoyl dehydrogenase. The vanadate (IV) formed reacted with hydrogen peroxide generated by using molecular oxygen to produce an OH radical. This free radical generation is responsible for the toxic effects of V.

Though Ti has been regarded as a biologically inert material, a long-term clinical study of metal ion release from titanium-based prosthetic segmental replacements of long bones in baboons by Woodman et al.\textsuperscript{16} identified potential haematologic and metabolic toxicity. There have also been case reports of Ti as a potential allergen.\textsuperscript{18-20} The aluminium ion is known to affect the metabolic activity of osteoblasts by hindering their proliferation and differentiation.\textsuperscript{23}

Many brands of mini-implants are currently available. Though various factors might direct the clinician to his or her choice of implant, few studies offer information on corrosion resistance and subsequent ion release from commercially available mini-implants.\textsuperscript{14,33}

Therefore, the present study was designed to evaluate the composition, surface microstructure and ion release from five commonly-used brands of available mini-implants. In an attempt to standardise the study selection, only a small headed mini-implant with a fixed length of 6 mm, a diameter of 1.5 mm and with a conical thread was chosen. However, head design varied from brand to brand.

The composition and microstructure were studied using the FEI Quanta FEG 200 - High Resolution Scanning Electron Microscope, equipped with an Energy Dispersive Spectrometer. In addition to the expected Ti, Al and V elements, carbon was also detected. Since surface inhomogeneity also contributes to an acceleration of ion release,\textsuperscript{37} the SEM study was performed before and after immersion in artificial saliva. As a conductor, the sample did not warrant metal coating prior to SEM analysis. This minimised the possibility of the elements of interest being masked during the EDAX analysis.

Although this was an in-vitro study, in order to simulate clinical scenarios in which different numbers of mini-implants may be used, the 10 mini-implants from each brand were divided into four sub-groups containing one, two, three, and four mini-implants each. Since the composition of the saliva has a significant effect on the corrosion process, Fusayama-Meyer artificial saliva\textsuperscript{38} was used. Based on the study by Holland in 1992,\textsuperscript{39} the electrolytes of this solution have been shown to closely mimic the electrochemical behaviour of natural saliva towards dental alloys and the results have been consistent with the clinical observations. It is also one of the most commonly used artificial saliva solutions in previous in-vitro corrosion studies.\textsuperscript{38} The normal salivary pH value ranges from 6.0 to 7.0\textsuperscript{40} but falls during orthodontic therapy.\textsuperscript{41} Hence, the pH was fixed at 5.8 following the guideline of a previous corrosion study by Knutson et al.\textsuperscript{38} Animal studies have found that peak levels of Ti and V were reached at four weeks after implantation\textsuperscript{15} and so the duration of the present study was set at 30 days.

The interpretation of the SEM images, after being in contact with artificial saliva for a month, were similar to the in-vivo findings of Sebbar et al.\textsuperscript{29,30} in which the surface microstructure of a new, as-received mini-implant was compared with retrieved mini-implants using optical microscopy. Inductively Coupled Plasma - Optical Emission Spectrometry was preferred to atomic absorption spectrometry as it detects the heavy metals without the
interference of other ions, by extracting each metal simultaneously, after pretreatment. The equipment has higher sensitivity and a wider range of linearity in the calibration curves. This permitted the detection of low levels of titanium, aluminium and vanadium ions.

The results revealed that there was a statistically highly significant variation in the release of Ti, Al and V between the groups. Groups 1, 2 and 3 showed no detectable V ion release, while Groups 2 and 3 did not have detectable Ti release. Moreover, Groups 2 and 3 revealed minimal change in their surface microstructure before and after their immersion in artificial saliva compared with the other groups. Wherever detectable amounts of Ti, Al and V ions were elicited, the ion release increased commensurate with the increase in the number of mini-implants. This was the trend in all groups except Group 3, in which Al release was greater in sub-group ‘c’ than in sub-group ‘d’. The maximum release of all three ions was seen in Group 4. It is interesting to note that the SEM images of Group 4 showed the most prominent pitting type corrosions post immersion, principally at sites of machining defects.

Vanadium is expected to be released in lesser amounts when compared with Ti and Al ions since it does not take part in the formation of the surface oxide layer. The results of the present study were consistent as the measured V values in all groups were appreciably less than those of Ti and Al values. Although the amount of vanadium release from all the groups was less than the dose at which vanadium exerts its cytopathic effects, it does not diminish the prospect of V ions being potentially toxic due to the small difference between the essential and toxic doses.

Another noteworthy finding was that Groups 1 and 4 had the highest ion release, especially of Ti and Al, and also the highest carbon content in the characterisation. Further studies may be appropriate to investigate the effect of carbon in influencing ion release.

There has only been one human study that has evaluated ion release from mini-implants placed in orthodontic patients. The values obtained were much less than those in the present study. It is difficult to directly compare the ion release values because of the in-vitro nature of the present study. The higher values seen in the present study could be attributed to the lack of saliva turnover in the in-vitro situation. The present study showed that even though the composition of the various brands of implants was similar, some performed better than others in relation to toxic ion release and surface microstructure alterations. The discerning clinician is advised to consider these factors when choosing a mini-implant. The increase in ion release when the number of implants is increased should also direct the clinician to the judicious use of mini-implants.

A mini-implant in the oral environment will be subjected to many solutions, such as blood, saliva and interstitial fluid as well as consumables. It is difficult to duplicate this situation experimentally. However, the present study, conducted in a controlled laboratory setting, facilitated the evaluation of mini-implants without the confounding factors of orthodontic appliances and environmental influences. Although the level of ion release fell below the levels needed to exhibit cytotoxic effects, there is still scope for further research to evaluate other commercially-available implants along with cytotoxic studies to determine and confirm the adverse effects of ion release.

**Conclusion**

Although all samples of the mini-implants had similar metal percentage content, Groups 2 and 3 performed better with respect to ion release and surface microstructural alterations. The ions released from all of the groups were lower than their respective toxicity levels.

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**References**

1. Daskalogiannakis J. Glossary of orthodontic terms. Leipzig: Quintessence Publishing Co., 2000.
2. Kanomi R. Mini-implant for orthodontic anchorage. J Clin Orthod 1997;31:763-7.
3. Hong RK, Heo JM, Ha YK. Lever-arm and mini-implant system for anterior torque control during retraction in lingual orthodontic treatment. Angle Orthod 2005;75:129-41.
4. Herman RJ, Currier GF, Miyake A. Mini-implant anchorage for maxillary canine retraction: a pilot study. Am J Orthod Dentofacial Orthop 2006;130:228-35.
5. Park YC, Lee SY, Kim DH, Jee SH. Intrusion of posterior teeth
using mini-screw implants. Am J Orthod Dentofacial Orthop 2003;123:690-4.
6. Baik UB, Chun YS, Jung MH, Sugawara J. Protraction of mandibular second and third molars into missing first molar spaces for a patient with an anterior open bite and anterior spacing. Am J Orthod Dentofacial Orthop 2012;141:783-95.
7. Velo S, Rotunno E, Cozzani M. The implant distal jet. J Clin Orthod 2007;41:88-93.
8. Jeon YJ, Kim YH, Son WS, Hans MG. Correction of a canted occlusal plane with miniscrews in a patient with facial asymmetry. Am J Orthod Dentofacial Orthop 2006;130:244-52.
9. Lin JC, Liu EJ, Yeh CL, Evans CA. A comparative evaluation of current orthodontic miniscrew systems. World J Orthod 2007;8:136-44.
10. Corrêa-Peres FA, Quaglio CL, Peralta RP, Carvalho PE, Siqueira DF. Metallographic analysis of the internal microstructure of orthodontic mini-implants. Braz Oral Res 2010;24:438-42.
11. Moraes LS, Serra GG, Müller CA, Andrade LR, Palermo EFA, Elias CN et al. Titanium alloy mini-implants for orthodontic anchorage: immediate loading and metal ion release. Acta Biomater 2007;3:331-9.
12. Danaei SM, Safavi A, Rooinpeikar SM, Oshagh M, Irannouri S, Omidkhoda M. Ion release from orthodontic brackets in 3 mouthwashes: an in-vitro study. Am J Orthod Dentofacial Orthop 2011;139:730-4.
13. Natarajan M, Padmanabhan S, Chitharanjan AB, Narasimhan M. Evaluation of the genotoxic effects of fixed appliances on oral mucosal cells and the relationship to nickel and chromium concentrations: an in-vivo study. Am J Orthod Dentofacial Orthop 2011;140:383-8.
14. Kerouso H, Moe G, Kleven E. In vitro release of nickel and chromium from different types of simulated fixed orthodontic appliances. Angle Orthod 1999;65:111-6.
15. de Moraes LS, Serra GG, Albuquerque Palermo EF, Andrade LR, Müller CA, Meyers MA et al. Systemic levels of metallic ions released from orthodontic mini-implants. Am J Orthod Dentofacial Orthop 2009;135:522-9.
16. Pithon MM, Santos RL, Martins FO, Medeiros PJ, Romanos MT. Citotoxicity of orthodontic mini-implants. Rev Clín Pesq Odontol. 2010;6:141-6.
17. Malkoç S1, Öztürk F, Çörekçi B, Bozkurt BS, Hakki SS. Real-time cell analysis of the cytoxicity of orthodontic mini-implants on human gingival fibroblasts and mouse osteoblasts. Am J Orthod Dentofacial Orthop 2012;141:419-26.
18. du Preez LA, Bülow KW, Swart TJ. Implant failure due to titanium hypersensitivity/allergy – Report of a case. SADJ 2007;62:22-5.
19. Sicilia A, Cuesta S, Coma G, Arregui I, Guiasola C, Ruiz E et al. Titanium allergy in dental implant patients: a clinical study on 1500 consecutive patients. Clin Oral Implants Res 2008;19:823-5.
20. Egusa H, Ko N, Shimazu T, Yatani H. Suspected association of an allergic reaction with titanium dental implants: a clinical report. J Prosthet Dent 2008;100:344-7.
21. Lin W, Stayton I, Huang Y, Zhou X-D, Ma Y. Cytotoxicity and cell membrane depolarization induced by aluminium oxide nanoparticles in human lung epithelial cells A549. Toxicol Environ Chem 2008;90:983-96.
22. Rogers MA, Simon DG. A preliminary study of dietary aluminium intake and risk of Alzheimer's disease. Age Ageing 1999;28:205-9.
23. Boyce BF, Byars J, McWilliams S, Mocan MZ, Elder HY, Boyle IT et al. Histological and electron microprobe studies of mineralisation in aluminium-related osteomalacia. J Clin Pathol 1992;45:502-8.
24. Heinemann G, Fichtl B, Vogt W. Pharmacokinetics of vanadium in humans after intravenous administration of a vanadium containing albumin solution. Br J Clin Pharmacol 2003;55:241-5.
25. Rodríguez-Mercado JJ, Roldán-Reyes E, Altamirano-Lozano M. Genotoxic effects of vanadium (IV) in human peripheral blood cells. Toxicol Lett 2003;144:359-69.
26. Rae T. The biological response to titanium and titanium-aluminium-vanadium alloy particles. Part II. Long-term animal studies. Biomaterials 1986;7:37-40.
27. Agency for Toxic Substances and Disease Registry 2012. ToxGuide. <http://www.atsdr.cdc.gov/toxguides/toxguide-58.pdf>
28. Blaya MG, Blaya DS, Mello P, Flores EM, Hirakata LM. Titanium alloy miniscrews for orthodontic anchorage: an in vivo study of metal ion release. Rev Odonto Cienc 2011;26:209-14.
29. Sebbar M, Bourzgui E, Azzab B, Elquars F. Anchorage miniscrews: a surface characterization study using optical microscopy. Int Orthod 2011;9:325-38.
30. Sebbar M, Bourzgui E, Lazzak L, Azzab B, El Quars F. [Microscopic comparison of the miniscrew's surface used in orthodontics: before and after use]. Rev Stomatol Chir Maxillofac 2012;113:365-9. French.
31. Kuphasuk C, Oshida Y, Andres CJ, Howijstra ST, Barco MT, Brown DT. Electrochemical corrosion of titanium and titanium-based alloys. J Prosthet Dent 2001;85:195-202.
32. Bordji K, Jouzeau JY, Mainard D, Payen E, Netter P, Rie KT et al. Cytocompatibility of Ti-6Al-4V and Ti-5Al-2.5Fe alloys according to three surface treatments, using human fibroblasts and osteoblasts. Biomaterials 1996;17:929-40.
33. Khan MA, Williams RL, Williams DF. The corrosion behavior of Ti-6Al-4V, Ti-6Al-7Nb and Ti-13Nb-13Zr in protein solutions. Biomaterials 1999;20:631-7.
34. Hanawa T. Metal ion release from metal implants. Material Science and Engineering C 2004;24:745-52.
35. Shl XL, Dalal NS. NADPH-dependent flavoenzymes catalyse one electron reduction of metal ions and molecular oxygen and generate hydroxyl radicals. FEBS 1990;276:189-91.
36. Woodman JL, Jacobs JJ, Galante JO, Urban RM. Metal ion release from titanium-based prosthetic segmental replacements of long bones in baboons: a long-term study. J Orthop Res 1984;1:421-30.
37. Strietzel R, Hösch A, Kalßfleisch H, Buch D. In vitro corrosion of titanium. Biomaterials 1998;19:1495-9.
38. Knutson KJ, Berzins DW. Corrosion of orthodontic temporary anchorage devices. Eur J Orthod 2013;35:500-6.
39. Holland RL. Corrosion testing by potentiodynamic polarization in various electrolytes. Dent Mater 1992;8:241-5.
40. Guyton, Hall JE. Textbook of medical physiology, 13th Ed. Philadelphia: Elsevier Publishers, 2016;740, Table 64-1.
41. Zabokova-Bibilova E, Sorirovska-Ivkovska A, Kanukova L, Pandilova M. The effect of orthodontic treatment on pH, buffer capacity and levels of Streptococcus mutans and lactobacillus. Somatologisk vjesnik 2012:93-7.
42. Huang TH, Yen CC, Kao CT. Comparison of ion release from new and recycled orthodontic brackets. Am J Orthod Dentofacial Orthop 2001;120:68-75.