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# Antibacterial Effect Of Nanocoating Of Orthodontic Archwires - A Systematic Review

Review Article

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## Abstract

**Aim:** To evaluate the antimicrobial effect of nanocoated orthodontic archwires.
**Materials and Methods:** A systematic review was conducted using the available electronic data bases which analysed the microbial adhesion after nano coating of orthodontic archwires against uncoated archwires. Due to the paucity of *in vivo* studies, invitro studies also were considered. Downs and Black checklist was used for risk of bias assessment. Data extraction was performed from each study and the results were tabulated.
**Results:** 6 studies which fulfilled the inclusion criteria were selected. Risk of bias assessment showed a medium to high risk of bias for most of the studies. The antibacterial effect of various nano coatings on the archwires were analysed.
**Conclusion:** Most studies included in the systematic review showed medium risk of bias. Due to the severe diversity of the methods used to assess the antimicrobial action, a metanalysis was not possible. For further understanding of nanoparticles, their use and their antimicrobial action, *in vitro* studies with a low risk of bias and RCTs are required before they can be adopted for routine clinical practice.

**Keywords:** Microbial Adhesion; Nanocoating; Nano Particles; Orthodontic Archwire.

## Introduction

Orthodontic appliances attract microorganisms and may cause periodontal problems or caries in the form of white spot lesions due to surface decalcification of the enamel. A study by Tufecki et al [1] states there is a 46% prevalence of white spot lesions in people undergoing orthodontic treatment for 12 months. Another study by Ritesh Gupta et al [2] also concludes that the amount of white spot lesions increases up to a prevalence of 25% for people having orthodontic treatment for over a year.

A study by Fatma Broke et al., [3] states that fixed orthodontic treatment results in dental plaque accumulation and gingival inflammation, increase in Plaque Index (PI) and Gingival Index (GI) as from the start of orthodontic therapy. A study by Liu et al [4] states orthodontic appliances form a conducive environment for factors causing gingival diseases and there is a significant increase in the number of bacteria during orthodontic treatment which reduced after removal of the appliance.

A number of surface coating of the archwires have been tried to mitigate the impact of these microorganisms on the tooth and gingiva during orthodontic treatment. A newer technology is the use of nano particles (NP) for their antibacterial property.

Nano particles are materials which are in the range of 0.0000001mm or 10-6mm in size. Due to their antibacterial property, they have been used in coating medical equipment like implantable devices as in heart valves and catheters. They are also used along with drug delivery devices which are implanted in the body. The antibacterial effects of nanoparticles are not yet clear-

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ly understood but oxidative stress induction, metal ion release, and non-oxidative mechanisms are being considered as possible mechanism of action [4].

A novel idea of utilising this antimicrobial property of nanoparticles on orthodontic archwires as a coating has the potential to reduce the number of microbes it harbours and hence reduce the incidence of white spot lesions and periodontal problems in people undergoing orthodontic treatment.

This systematic review aims to compile and summarise the antimicrobial effect of nanoparticle coated orthodontic archwires.

## Materials and Methods

This systematic review is structured in accordance to the PRISMA [6] (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).

### Eligibility criteria

**Population:** Studies involving the use of an orthodontic arch wire.
**Intervention:** Studies involving nanocoating of orthodontic archwires.

### Comparator

Studies comparing uncoated archwires with nanocoated archwires. Studies comparing two nanocoated archwires are not included in the study.

### Outcome

Studies evaluating antimicrobial activity or colony counts as their primary outcomes and friction and roughness as secondary outcomes were included.

### Study design

Randomised control trials, Prospective controlled clinical trials and *in vitro* studies were included. Case reports, case series and descriptive studies, review articles, opinion articles were excluded.

Articles in English were only included.

The PICO protocol of the studies included is presented in table 1.

### Search strategy

A comprehensive search was done in the electronic search engine using PubMed, Scopus, Google scholar, Cochrane clinical trials, Web of science, Embase and Medline databases without limitations to identify eligible articles.

The initial search was carried out on August 2020 and was repeated on September 2020 to finalise before writeup.

The search was further expanded to major orthodontic journals like American Journal of orthodontics and dentofacial orthopaedics, Angle Orthodontist, Journal of clinical orthodontics, European journal of orthodontics and Journal of Indian orthodontic society. References and related articles were hand checked using electronic search engines in case they got missed out during the above procedures.

Two reviewers independently scanned the titles of the articles which were identified by electronic as well as manual search and decided whether it was relevant to the study.

The abstract of the articles was carefully as well as critically analysed to identify studies that met our inclusion criteria. If a consensus about inclusion of a study was not obtained between the two authors, a third reviewer was consulted with.

PRISMA flow chart for the systematic review is presented in figure 1.

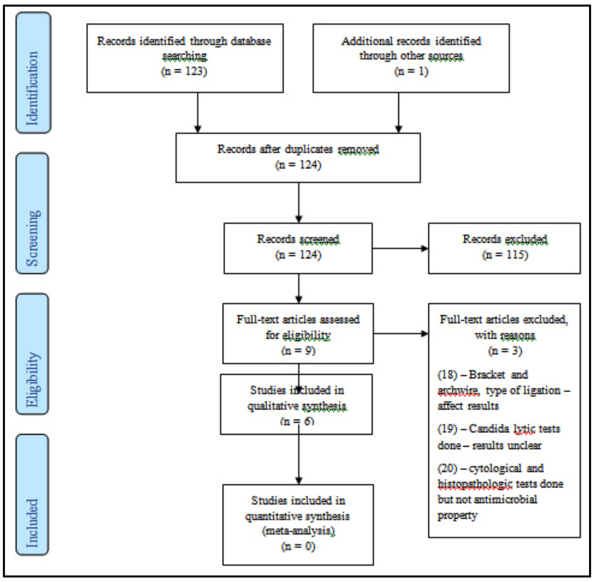
### Risk of Bias assessment

Since the systematic review included both randomised and non-randomised studies, Downs and black check list [7] was used for

**Table 1. PICO.**

| Study | Population | Intervention | Control | Outcome | Study |
|---|---|---|---|---|---|
| Mhakse et al, 2015 [7] | Archwires | Silver nanocoated SS and NiTi | Uncoated SS and NiTi | CFU<br>Microbial adhesion by weight change | *In vitro* |
| Keerthi Venkatesan et al, 2020 [8] | archwires | 0.016” NiTi with TiO2 nano coating | 0.016” uncoated NiTi | S. mutans adhesion by RT-PCR | Prospective clinical study |
| Kachoei et al, 2016 [9] | archwires | 0.016” SS with ZnO nano coating | 0.016” uncoated SS | Antibacterial activity by calorimetric method | *In vitro* |
| Javier et al, 2020 [10] | Archwire | Silver nanocoating | NiTi archwire | MIC | *In vitro* |
| Jiming Liu et al, 2017 [11] | Archwire | N Doped $TiO_2$ coated CAW | Uncoated CAW | CFU | *In vitro* |
| Hammad et al, 2020 [12] | Archwire | 0.016 x 0.022-in NiTi with ZnO coating | Uncoated 0.016 x 0.022-in NiTi wires | Antibacterial activity by inhibition zone | *In vitro* |

**Figure 1. PRISMA Flow diagram.**




assessing the risk of bias for each study.

Scoring was done for each article and were evaluated as excellent (25-28) or good (20-24) or fair (15-19) or and poor (≤14). The risk assessment was done independently by two authors. In case of any disagreement between the authors, a third author was consulted with.

Due to the high heterogenicity in the type of nano coating used and the methods used to assess its antimicrobial activity in the studies included in the systematic review, a meta-analysis was not possible.

### Data Extraction

After eliminating the duplicates, full texts were obtained for the all the studies which were eligible for the study. Two authors independently extracted the data form the articles. Sample size, nano coating used, method of antibacterial activity, amount of antimicrobial action was tabulated.

## Results

Electronic data search received 123 results in the online data bases that were available by using the MeSH terms Archwires AND orthodontics AND nanocoating AND antibacterial action. Manual searching was also done for articles matching the inclusion criteria. After removing the duplicates, we ended up with 124 studies. The studies were then screened based on the abstract for relevancy to the research question, after which 115 studies were excluded as they did not meet with the inclusion criteria.

Full texts were obtained for the remaining 9 articles and 3 of them was excluded. In the studies [18] brackets and archwires were nanocoated and hence there is a chance of altered results, [19] did candida lytic tests but the results are unclear and [20] compared cytotoxic and histologic properties but not antimicrobial. Finally, 6 studies which fulfilled the eligibility criteria were included in the systematic review.

### Risk of bias

Risk of bias was done for all the 6 studies which were included in the systematic review. Bias assessment was done using Downs and Black check list, as both in-vivo and in-vitro studies were included in the study. The results are summarised accordingly in table 2.

### Data Extraction

Of the six studies reviewed, antimicrobial activity of silver nano coating was assessed in 2 studies - [8] and [11], Titanium oxide was used in [9] and [12], and zinc oxide nano coating was utilised in [10] and [13]. The sample size and the results of the various studies along with their methods are tabulated in table 3. The roughness or friction estimation is summarised in table 4.

## Discussion

In this systematic review various nanocoating on archwires and their antibacterial and anti-adherence property was studied. Nanocoating is an innovative and a novel method of decreasing the microbial load on a substrate by coating. By nano coating archwires, the reduction in the microbial load can be equated to the decrease in the incidence of white spot lesions and the incidence of periodontal problems. The most commonly used nanocoatings for orthodontic archwires are silver, titanium oxide and zinc oxide nano coatings.

Due to the high heterogenicity in the methods used in the above studies, comparison between the three nano coatings and also a meta-analysis is not possible.

### Silver nanocoating

Silver was used as a disinfectant for several millennia and as salt in colloidal systems (silver nitrate) during the late 1900s for its antibacterial property. Comprehensive research on the antibacterial action of Ag NPs emerged around the start of the 21st century. The advantage of silver nano particle is that, it possesses high antibacterial activity against a broad range of microbes even in small concentrations. At such concentrations, systemic toxicity of silver is not possible and is economical also.

**Table 2. Risk of Bias assessment.**

| Assessment | Mhakse et al, 2015 (7) | Keerthi Venkatesan et al, 2020 (8) | Kachoei et al, 2016 (9) | Javier et al, 2020 (10) | Jiming Liu et al, 2017 (11) | Hammad et al, 2020 (12) |
|---|---|---|---|---|---|---|
| Aim | 1 | 1 | 1 | 1 | 1 | 1 |
| Outcomes | 1 | 1 | 1 | 1 | 1 | 1 |
| Inclusion criteria | 1 | 1 | 0 | 1 | 1 | 1 |
| Interventions | 1 | 1 | 1 | 1 | 1 | 1 |
| Confounders | 0 | 1 | 0 | 0 | 0 | 0 |
| Main outcomes described? | 1 | 1 | 1 | 1 | 1 | 0 |
| Estimates of random variability | 1 | 1 | 1 | 1 | 0 | 1 |
| ADR reporting | 0 | 0 | 0 | 0 | 0 | 0 |
| Attrition reported? | 0 | 0 | 0 | 0 | 0 | 0 |
| Actual p-value reported? | 1 | 1 | 1 | 1 | 0 | 1 |
| Samples asked to participate represent a population | 0 | 1 | 0 | 0 | 0 | 0 |
| Samples prepared represent population | 0 | 1 | 0 | 0 | 0 | 0 |
| Samples from facility used? | 1 | 1 | 1 | 1 | 1 | 1 |
| Blind samples? | 1 | 0 | 1 | 1 | 1 | 1 |
| Researcher blinding? | 0 | 0 | 0 | 0 | 0 | 0 |
| Data dredging? | 1 | 1 | 1 | 1 | 1 | 1 |
| Length of follow up same? | 1 | 1 | 1 | 1 | 1 | 1 |
| Statistical tests used appropriate? | 1 | 1 | 1 | 1 | 1 | 1 |
| Compliance reliable? | 1 | 1 | 1 | 1 | 1 | 1 |
| Outcomes accurately measured? | 1 | 1 | 0 | 1 | 1 | 0 |
| Samples from same population? | 1 | 1 | 1 | 1 | 1 | 1 |
| Samples recruited at same time? | 1 | 1 | 1 | 1 | 1 | 1 |
| Randomisation? | 1 | 0 | 1 | 1 | 1 | 1 |
| Concealment of allocation | 0 | 0 | 1 | 0 | 0 | 0 |
| Adjustment of confounding factors? | 0 | 1 | 0 | 0 | 0 | 0 |
| Attrition taken into account | 0 | 0 | 1 | 0 | 1 | 1 |
| Power | 1 | 1 | 1 | 1 | 1 | 1 |
| Total | 18 | 20 | 18 | 18 | 17 | 17 |
| | Fair | Good | Fair | Fair | Fair | Fair |

The mechanism of action of silver nano particles can be attributed to its ability to accumulate at bacterial membrane and form aggregates, as silver ions, thus causing disruption of cell membrane integrity by formation of pores leading to cell death. This is due to the high affinity of silver ions to organic amines, phosphates and most notably thiols (sulphur containing groups) found in the cell membrane.

Formation of reactive oxygen species as also been considered as a prime mechanism of action. The high oxidative stress can cause cell inactivation [14]. The size of the nano particle may also have a role to play in its anti-bacterial activity. Smaller the size, greater is the internalisation and hence greater antimicrobial action. Silver nano particles can also cause DNA damage through interaction with the exocyclic nitrogen present in the adenine, guanine, and cytosine bases hence causing cell death [15]. The surface topography of the archwire is also altered by the nano coating preventing adhesion to the parent archwire.

The study by Mhaske et al, 2015 [8] states there is both an antibacterial activity and an anti-adhesion activity due to silver nano coating.The uncoated stainless-steel wires showed 35.4% increase in weight and silver nanocoated stainless steel wires showed only 4.08 % increase in weight. Uncoated nickel titanium wiresshowed 20.5 % increase in weight whereas silver nanocoated Nickel tita-

**Table 3. Data extraction for anti-microbial activity.**

| Study | Sample size and intervention | | Results | |
|---|---|---|---|---|
| | Control | Experimental | Control | Experimental |
| Mhakse et al, 2015 [7] | a) 20 Uncoated NiTi archwires | 20 Silver nano coated NiTi archwires | CFU - 836.60 ± 48.97 Wt diff - 0.085 ± 0.024 | CFU - 220.90 ± 30.73Wt diff - 0.010 ± 0.020 |
| | b) 20 Uncoated SS archwires | 20 Silver nano coated SS archwires | CFU - 748.90 ± 35.64Wt diff - 0.045 ± 0.028 | CFU - 203.20 ± 41.94Wt diff - 0.010 ± 0.021 |
| Keerthi Venkatesan et al, 2020 [8] | 12 uncoated archwires | 12 $TiO_2$ nanocoated archwires | PCR -Ct - 37.00 ± 6 1.90 | PCR -Ct - 30.97 ± 6 2.23 |
| Kachoei et al, 2016 [9] | 8 uncoated NiTi archwires | 8 ZnO nano coated archwires | Positive for bacterial growth by calorimetric test | Negative for bacterial growth by calorimetric test |
| Javier et al, 2020 [10] | uncoated NiTi in CHX as positive control | Ag coated NiTi | MIC<br>S. mutans - 300 ± 111.80µg/mL<br>L. acidophilus - 450 ± 111.80µg/mL | MIC<br>S. mutans - 60 ± 22.36µg/mL<br>L. acidophilus - 15 ±5.59µg/mL |
| Jiming Liu et al, 2017 [11] | CAW | $TiO_2$<br>N – Doped $TiO_2$ | Reduction in colonies0.9% | Reduction in colonies5.9%<br>87.2% |
| Hammad et al, 2020 [12] | 12 – uncoated NiTi wires | 12 – ZnO coated NiTi wires | - | Inhibition zone diameter<br>4.25 ±0.49<br>6.25 ±0.64<br>3.57 ±0.43 |

**Table 4. Roughness/Friction estimation.**

| Study | Sample used | | Results | |
|---|---|---|---|---|
| | Control | Experimental | Control | Experimental |
| Mhakse et al, 2015 [7] | a) 20 Uncoated NiTi archwires | 20 Silver nano coated NiTi archwires | Did not estimate | |
| | b) 20 Uncoated SS archwires | 20 Silver nano coated SS archwires | | |
| Keerthi Venkatesan et al, 2020 [8] | 12 uncoated archwires | 12 TiO2 nanocoated archwires | 0 day - 1591.08 ± 260.41nm | 0 day - 746.14 ± 150.45 nm |
| | | | 30 days - 2296.18 ± 730.93 nm | 30 days -1922.04 ± 1007.81 nm |
| Kachoei et al, 2016 [9] | 8 uncoated NiTi archwires | 8 ZnO nano coated archwires | 1.412 ± 0.11N | 1.227 ± 0.13N |
| Javier et al, 2020 [10] | uncoated NiTi | Ag coated NiTi | Did not estimate | |
| Jiming Liu et al, 2017 [11] | CAW | $TiO_2$<br>N – Doped $TiO_2$ | Did not estimate | |
| Hammad et al, 2020 [12] | 12 – uncoated NiTi wires | 12 – ZnO coated NiTi wires | Frictional load 1.568 N | Frictional load 1.169 N |

nium wires showed 4.4 % increase in weight.But the reason for the anti-adherence property of silver nanocoating was not specified in the study. A study by Shah et al, 2018 [16] states there is a reduction in the friction of silver nanocoated stainless steel archwires which may be attributed to the reduction in the adherence of the microbes.

The Silver nanoparticles exhibited better bacteriostaticand bactericidal effect with concentration less than five-fold as compared to chlorhexidine [11]. Although it produces additive effect with antibiotics like amoxicillin and clindamycin, resistance can develop to silver nano particles also.

The silver coating on wires is a surface modification and hence is prone to wear duringarchwire sliding. The durabilityand sustainability of silver coatings under clinical situationsin the oral environment must also be studied before these archwires are commercialised.

### Titanium nanocoating

$TiO_2$ is a thermally stable and biocompatible chemical compound with high photocatalytic activity that has good antimicrobial action.Titanium dioxide nanoparticles ($TiO_2$ NPs) are of particular interest due to its particular abilities, such as bactericidal photocatalytic activity.The main photocatalytic characteristic of $TiO_2$ is a wide band gap of 3.2 eV, which can trigger the generation of high-energy electron–hole pair under UV-A light with wavelength of 385 nm or lower. This generates ROS except it is under a nanoscale.The nanoscale enables easy penetration of the cell wall and cell membrane, enabling the increase of the intracellular oxidative damage.

The formed ROS can affect the microbes by destroying the cell wall and cell membrane causing increase in the membrane fluidity, leakage of cellular content, and eventually cell lysis. The antimicrobial effect of $TiO_2$ nanoparticles is more effective on gram positive bacteria than gram negative due to its differences in cell wall morphology. $TiO_2$ NPs can oxidize components of cell signalling pathways orinterfere the transcription factors changing the genetic expression. It can also affect the assimilation and transport of iron and inorganic phosphates leading to loss of homeostatic regulation,secondary metabolites production [16].

Keerthi Venkatesan et al, 2020 [9] determined the antibacterial effect of $TiO_2$ nano particles using RT-PCR test by measuring the cycle threshold (Ct). The Ct value is inversely proportional to theamount of bacterial genome present, meaning, the higher the Ct value, lesser is the bacterial load and hence more the antibacterial effect.The nanocoated archwires have greater Ct value than that of uncoated archwires indicating antimicrobial action of $TiO_2$ nanoparticles. They also found a moderate positive correlation between Ct valueand Ra of 0.016-in NiTi wires and a moderate negativecorrelation between 0.016-in $TiO_2$ nanoparticle coatedNiTi wires and Ct value indicating smoother surface of the wire has some anti-adherence property also.

The study by Jiming et al [11] compared CAW, $TiO_2$ and N – Doped $TiO_2$ for antibacterialaction and found that there is only 5.9% reduction in the colonies using $TiO_2$ alone against 87.2% in N-doped $TiO_2$. This may be due to the fact that ROS formation requires UV light. The UV filter and presence of visible light activated N doped $TiO_2$ nanoparticles only and thus the difference in antibacterial action.

The studies show the need for activation of the $TiO_2$ by light for proper action against the microbes. The photocatalytic effect requires more invivo studies where activation conditions may be varied than invitro studies.

### Zinc oxide nano coating

Zinc oxide nanoparticles inhibits the growth of microorganisms by permeating into the cell membrane hence the antibacterial activity. The oxidative stress damages lipids, carbohydrates, proteins, and DNA. Lipid peroxidation leads to alteration in cell membrane which eventually disrupt vital cellular functions. Disrupted bacterial cell membrane integrity, reduced cell surface hydrophobicity, and downregulation of the transcription factors for oxidative stress-resistance genes in bacteria eventually lead to cell death. They also enhance intracellular bacterial killing by inducing ROS production. These nanoparticles disrupt biofilm formation and inhibit hemolysis by hemolysin toxin produced by pathogens [17].

Kachoei et al, 2016 [9] stated there is antimicrobial activity by ZnO nanocoating but the test was a qualitative calorimetric test. Quantitative antimicrobial estimation was not done. However, the anti-adherent property can be due to the antimicrobial property and the reduction in the surface roughness of the ZnO nanocoating. Also, the mechanical properties of ZnO coating protects the wire from pitting and corrosion and hence surface prevents adhesion of microbes to the cracks in the wire.

The results of Hammad et al, 2020 [12] are also in accordance to the results of Kachoei et al and there is a reduction in microbial load and also 34% reduction in friction contributing to anti-adherence property of the nanocoating.

## Conclusion

Most of the studies included in the systematic review were assessed fair in risk of bias assessment. Due to the various methods used to check the antimicrobial property, a metanalysis and comparison between the different methods was not possible. Nanocoating in orthodontics is still in its infancy and further understanding of the nanoparticles, their mechanism of action, cytotoxicity in human tissues is required.High standard research with low risk of bias preferably in vivo studies like RCT is necessary before nanocoatings can be adopted in routine clinical practice.

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