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THE EFFECT OF CAFFEINE IN COCOA ON TOOTH MOVEMENT IN ORTHODONTIC TREATMENT

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ABSTRACT

Background: The use of orthodontic appliances for a long time makes it difficult to maintain oral hygiene, so that patients are more susceptible to caries and periodontal disease. Currently, natural ingredients have been used to accelerate tooth movement, one that can be used is the caffeine contained in cocoa. Caffeine can reduce the levels of osteoblasts, Alkaline Phosphatase (ALP), and Osteoprotegerin (OPG) where OPG can inhibit the differentiation and activity of osteoclasts. In addition, caffeine can increase the Receptor Activator of Nuclear factor-Ligand (RANKL), which functions to form and activate osteoclasts, thereby accelerating tooth movement. **Purpose**: This study aims to determine the effect of caffeine content in cocoa on tooth movement in orthodontic treatment **Methods:** Analyzed three (3) journals from Google Scholar, PubMed, and ResearchGate. The journal analyzed was the effect of caffeine content in cocoa on tooth movement in orthodontic treatment and the effect of dose and duration of caffeine consumption from chocolate on alveolar bone mineral density on orthodontic tooth movement. **Conclusion**: This review proves that cocoa contributes to active orthodontic treatment by modulating the rate of tooth movement, inducing osteoclast genesis, and ultimately shortening the duration of orthodontic treatment. Further studies are needed at the clinical level to confirm the efficacy and potential of cocoa in accelerating tooth movement in orthodontic patients.

INTRODUCTION

Orthodontic movement of teeth occurs due to remodeling of alveolar bone and periodontal tissue. Bone remodeling requires the coordination of three types of bone cells, namely, osteoblasts, osteocytes, and osteoclasts. During the movement of orthodontic teeth, bone mineral density is regulated by osteoblast and osteoclast cells through interactions between *receptor activator of nuclear factor-ligand (RANKL*), receptor activator of nuclear factor-κB *(*RANK), and *osteoprotegerin* (OPG). Osteoblasts act as bone-forming cells, while

osteoclasts absorb alveolar bone. The proliferation of osteoblasts from bone formation is identified by increased expression of *alkaline phosphatase* (ALP). Osteoclasts are regulated by two main cytokines*, macrophage colony-stimulating factor* (M-CSF) and RANKL produced by osteoblasts that bind to osteoclast receptors, namely c-Fms and RANK (Arianda *et al*., 2021; Arnanda *et al*., 2020).

The long period of use of orthodontic appliances makes it difficult to maintain cleanliness mulut, so patients are more susceptible to caries and periodontal disease. Lately, natural ingredients have been used, developed and produced for treatment purposes, one of which is consuming caffeine in chocolate to speed up the movement of teeth. It reduces bone mineral density (BMD) by lowering vitamin D receptor (VDR) expression. Caffeine can also reduce the differentiation of mesenchymal stem cells (MSCs) into osteoblasts by reducing binding *ALPHA-1 Core Factor*(Cbfa1). A decrease in BMD can trigger accelerated bone remodeling thereby shortening the duration of orthodontic treatment. Giving chocolate during the active period of orthodontic treatment can also increase RANKL expression and decrease OPG on the compressed side which causes accelerated movement of orthodontic teeth (Arianda *et al*., 2021; Arnanda *et al*., 2020).

METHOD

This writing is made based on relevant reference sources obtained from articles, journals, *textbooks, and* websites *accessed through Google Scholar, Science Direct and PubMed, with keywords* "Caffeine", "Cocoa", "Tooth Movement"

Literature search is limited by inclusion criteria in the form of publication years 2017 to 2022, using English, full articles available, and according to the topic discussed. Literature is eliminated with exclusion criteria in the form of less relevant topics.

RESULT

The results found in the database searched are shown by the flow chart in Figure 1. A total of 44 references were found from the Google Scholar and PubMed databases. After analysis based on inclusion criteria, 10 were selected and 34 articles were excluded because they were not relevant to the topic. After 10 journals were read, there were 4 articles in the exclusion because these four articles were not relevant to the topic so that 6 articles were included in the integrative review (Table 1).

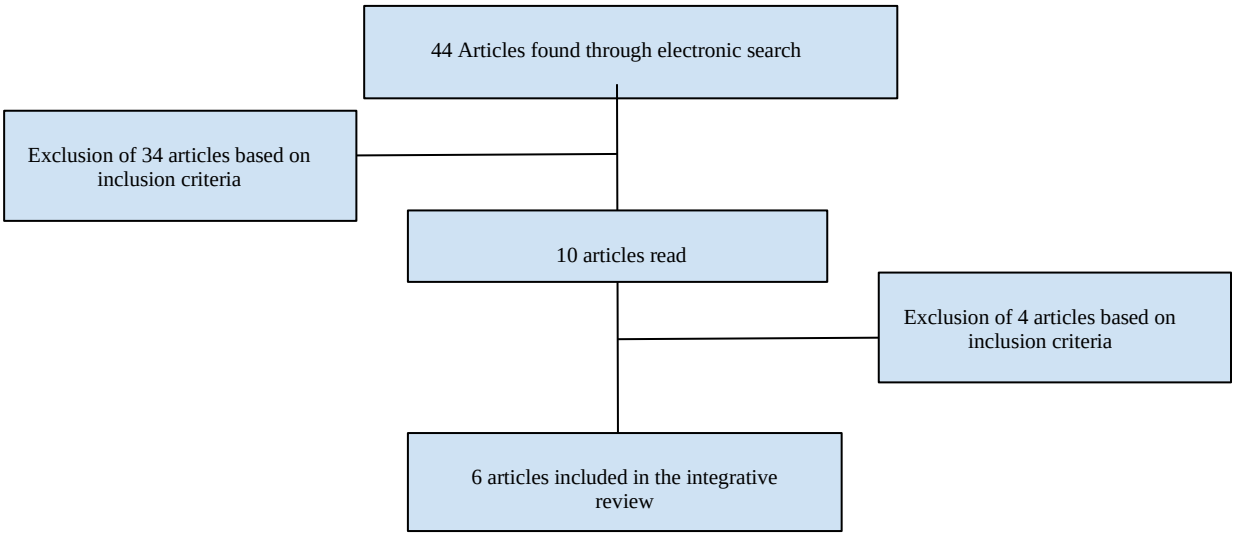

Figure 1. Flow Chart Publication of all *databases*

Table 1. Research Results of the Effects of Caffeine Content in Cocoa on Tooth Movement in Orthodontic Treatment (Arianda *et al*., 2021; Arnanda *et al.,* 2020; Alhasyimi *et al*., 2019; Alhasyimi *et al*., 2022; Shirazi M *et al*., 2017; Herniyati *et al*., 2018)

Reference	Purpose	Method	Sample	Result
Arianda *et al.,* 2021	The effect of cocoa administration on the number of osteoblasts and *alkaline phosphatase (ALP)* levels during orthodontic tooth movement in rats	24 male Sprague–Dawley rats were given 4.8 g of cocoa powder with 2.7 mg of caffeine. A three-spin stainless steel coil spring with an orthodontic force of 35 cN is stabilized on the incisor teeth of the upper jaw.	24 male Sprague–Dawley rats aged 10 weeks	The number of osteoblasts and ALP levels in the treatment group were significantly lower than in the control group.
Arnanda *et al.,* 2020	Effect of caffeine in chocolate (Theobroma cacao) on alveolar bone mineral density in guinea pigs (Cavia cobaya) with movement of orthodontic teeth	48 male guinea pigs aged 3-4 months with a body weight of 300-350 grams were divided into four groups. An open coil spring is applied to the mandibular inter-incisors.	48 male guinea pigs	Based on the results of the study, it can be concluded that caffeine consumption in chocolate does not reduce the mineral density of the alveolar bone of the lower jaw in guinea pigs (Cavia cobaya) with orthodontic tooth movement.
Alhasyimi *et al.,* 2019	Cocoa administration can accelerate the movement of orthodontic teeth by inducing osteoclastogenesis in mice	24 Sprague-Dawley rats, divided equally into two groups: cocoa and control. The upper incisor of all rodents is subjected to force orthodontic 35 cN and transferred to distal with coil spring 3-spin stainless steel. During OTM, cocoa groups were given 4.8 g unsweetened cocoa once a day.	24 male Sprague-Dawley rats aged 10 weeks	OPG levels were significantly lower on day 14 after orthodontic appliance installation and RANKL levels were significantly higher on days 0, 1, and 7 after orthodontic appliance installation in the cocoa group compared to the control group.
Alhasyimi *et al.,* 2022	evaluate the effect of cocoa administration during orthodontic tooth movement (OTM) on RUNX2, calcium levels, and osteoclast	48 Sprague Dawley is divided into four subgroups, given different levels of cocoa orally. The upper incisors of both groups are fastened with 3-	48 Sprague Dawley aged 10 weeks	RUNX2 levels and lacuna resorption depth differed significantly between groups, but daily administration of cocoa did not significantly lower calcium levels.

	bone absorption activity in mice.	spin loop springs that provide 35 g of orthodontic force .		
Shirazi *et al.*, 2017	To determine the effect of different doses of caffeine on the movement of orthodontic teeth (OTM) in mice.	40 male rats, Sprague-Dawley weighing 250-300 g. The rats were randomly assigned to 4 groups of 10 animals each and 1 g/l, 2 g/l and 3 g/l of caffeine were added to their drinks.	40 male rats, Sprague-Dawley weighing 250-300 g.	Significant decreases in OTM were observed only at 2 g/l (P=0.043) and 3 g/l (P<0.01). Number of osteoclasts and depth of resorption-lacunae showed significant differences between each caffeine group and control mice (P<0.05). None of the variables showed significant differences between the caffeine groups (P>0.05)
Herniyati *et al.* 2018	Analyze the effect of caffeine on PGE2 levels during orthodontic tooth movement.	16 healthy male rats were divided into 2 groups (control and treatment), caffeine 1.35 mg / 100 g body weight twice a day for 14 days	16 male rats (Spraque Dauwley) 250-300 grams	Caffeine on days 8 and 15 increases PGE2 levels in areas of compression and tension. PGE2 levels in the compression region are significantly greater than in the tensile region.

Tooth Movement

Orthodontic devices are devices used to correct dental malocclusion, so that good alignment of teeth, aesthetic functions and occlusion is obtained. Moving the teeth through the dentoalveolar complex is a synergistic sequence of changing tooth position and remodeling biological tissue. The process can be stimulated using mechanical forces obtained from the activation of components of orthodontic devices applied to the teeth and passed on to the tissues surrounding the teeth including the gingiva, periodontal ligaments and alveolar bone. Types of orthodontic tooth movement consist of tipping, bodily, rotation, extrusion and intrusion, and torque (Amin *et al*., 2017).

Gear movement mechanism

The continuous application of mechanical forces to the teeth will result in the remodeling of the alveolar bone as well as periodontal ligaments, and the movement of the teeth. Orthodontic movement is a process that involves the coordinated reaction of several cell types and various chemical mediators. The biological system of the teeth reacts to large variations in force, application time, and direction of coming force which ultimately results in bone remodeling and orthodontic tooth movement.[4,5,6,7.] The movement of teeth resulting from the application of mechanical force of orthodontic devices has three phases, namely the initial phase, lag phase and postlag phase (Amin *et al*., 2017).

Cacao

The results of orthodontic treatment can be achieved within 1-3 years. During long treatment periods, users of orthodontic appliances may experience complications and risks of orthodontic treatment, such as caries, white spot lesions, periodontitis, gingivitis, and root resorption. Efforts to accelerate orthodontic treatment need to be done to overcome the side effects of orthodontic treatment that are relatively long (Arianda *et al*., 2021).

Chocolate (*Theobroma cacao*) is a processed cocoa product that has a mixture

of various chemical compounds. Chocolate generally contains 55% fat, 17% carbohydrates, 11% protein, and the rest tannins. The amount of caffeine in chocolate varies based on the percentage of cocoa it contains, with 100% cocoa chocolate (unsweetened chocolate) containing about 240 mg of caffeine/100g, 55% of cocoa (bitter chocolate) containing 124 mg of caffeine/100g, and 33% of cocoa (milk chocolate) containing 45 mg of caffeine/100g. Exposure to the right dose of caffeine can affect orthodontic treatment (Arnanda *et al*., 2020).

The Effect of Caffeine Content in Cocoa on Tooth Movement

According to Arianda *et al*. in 2020, Caffeine can reduce Bone Mineral Density (BMD) by lowering the expression of Vitamin D Receptors (VDR). Caffeine can also reduce the differentiation of Mesenchymal Stem Cells (MSCs) into osteoblasts by lowering the alpha-1 core binding factor (Cbfa1). Exposure to the right dose of caffeine can inhibit the formation of osteoblast cells and cause a decrease in Bone Mineral Density (BMD) of Sprague-dawley mice. A decrease in bone mineral density can trigger accelerated bone remodeling to shorten the duration of orthodontic treatment. The proliferation of osteoblasts throughout bone formation is identified by increased expression of alkaline phosphatase (ALP). The use of caffeine 2.7 mg can decrease ALP activity where ALP is a marker of osteoblast activity during new bone formation on the alveolar bone (Arianda *et al*., 2021).

Based on research by Arnanda *et al* in 2020 revealed that the dose of caffeine used, which is 2.3 mg to 4.6 mg for 14 days, is safe for consumption and has a positive impact because it can accelerate the orthodontic movement of guinea pigs but does not cause a decrease in alveolar bone mineral density (Arnanda *et al*., 2020).

DISCUSSION

Cocoa is a natural material that is being consumed by people worldwide. The health benefits of cocoa have attracted significant attention from scientists. Interestingly, cocoa contains methylxanthine, an active compound that contains a large amount of caffeine. Daily ingestion of caffeine in coffee may contribute to the acceleration of tooth movement. Caffeine interrupts the Ca2+ ion balance, thereby leading to low bone density, and accelerates bone remodeling, thereby shortening orthodontic treatment duration. Cocoa significantly increases osteoclast bone absorption activity during active OTM. On the compression side, with light force, many of the many-nucleated osteoclasts in the Howship lacuna absorb the alveolar bone directly. The caffeine methylxanthine found in cocoa may facilitate the process. This caffeine in cocoa can cause apoptosis of osteoblasts by increasing the formation of reactive oxygen species due to increased production of cyclic adenosine monophosphate and an increase in the number of osteoclasts as well as surface resorption resulting in increased bone resorption. The use of caffeine to enhance orthodontic tooth movement (OTM) has been well-documented (Alhasyimi *et al*., 2019; Alhasyimi *et al*., 2022). These studies looked at the remodeling and resorption processes that occur during the movement process of orthodontic teeth.

During orthodontic tooth movement, bone mineral density is regulated by osteoblasts and osteoclast cells through interactions between nuclear factor-ligand receptor activator (RANKL), nuclear factor receptor-κ B activator (RANK), and osteoprotegerin (OPG). There is a correlation between osteoblasts and osteoclasts, which mediates osteoclastogenesis. Osteoclast-osteoblast communication contributes to the merging of bone resorption. The process of bone resorption begins with the bonding between the RANKL produced by osteoblasts and the RANK presented in the pre-osteoclast. RANKL further binds to RANK on the surface

of osteoclast precursors and recruits a protein adapter, which causes NF-kB activation and translocation to the nucleus. NF-kB increases cFos expression to trigger osteoclastogenic gene transcription, and eventually initiates the differentiation of osteoclast precursors into preosteclase cells. Conversely, increased levels of osteoprotegerin (OPG) produced by osteoblasts cause a decrease in RANKL levels and inhibit OTM. OPG is a natural receptor expressed by osteoblasts, which inhibit osteoclast differentiation and activity by binding to RANKL and blocking RANKL from interacting with RANK. A decrease in osteoblast differentiation is indicated by a decrease in OPG expression levels (Alhasyimi *et al*., 2019).

Previous research has shown that local RANKL gene transfer significantly accelerates OTM by increasing RANKL expression and increasing osteoclastogenesis. This is in line with the research of Alhasyimi *et al.,* 2019 and Arnanda *et al*., 2020. In the 2019 Alhasyimi et al study, the results of the group applied 4.8 grams of cocoa showed significantly high RANKL levels, low OPG levels and faster OTM than the group without cocoa. In this study, RANKL expression increased significantly and reached its highest level on day 7 after device installation, while OPG expression showed a downward trend after cocoa administration. These results show that cocoa administration during active OTM allows for a decrease in OPG levels and increases RANKL levels (Alhasyimi *et al*., 2019).

Alhasyimi et al in 2022 also conducted cocoa research on OTM as seen from RUNX2 levels. In this study, RUNX2 also played a role in increasing osteoclastogenesis. Changes in RUNX2 expression result in periodontal tissue reconstruction and gear position shifting. According to the findings, RUNX2 stimulates osteoclastogenesis and bone resorption via the AKT/NFATc1/CTSK axis. Increased osteoclastogenesis during the movement of orthodontic teeth facilitates the rapid movement of orthodontic teeth. RUNX2 can also trigger the expression of bone matrix genes, including osteocalcin and alkaline phosphatase, in the early stages of OTM. (Alhasyimi *et al*., 2022).

In addition, a study conducted by Herniyati et al in 2018 discussed Prostaglandins (PG), especially PGE2, which acts as an inhibitor or stimulator of bone metabolism, depending on physiological or pathological conditions. Anabolic effects occur primarily as a bone response to the application of mechanical force and fracture healing, whereas PGE2-mediated bone resorption increases bone loss in inflammatory diseases and in response to prolonged immobilization. PGE2 is a powerful bone resorption stimulator by enhancing replication and differentiation of osteoclast precursors. This study proved that caffeine administration increased PGE2 levels in pressure areas and strain areas compared to decaffeinated on day 8. This explains caffeine induces an increase in PGE2 release. In orthodontic tooth movement, caffeine works in two ways: increasing intracellular cAMP concentrations, and mediators regulating the inhibition of osteoblast proliferation, firstly caffeine inhibits phosphodiesterase that breaks down cAMP; caffeine both induces increased release of prostaglandin E2 (PGE2) in vitro and in vivo. High concentrations of PGE2 can increase intracellular cAMP in osteoblasts and also increase osteoclast activity (and inhibit collagen synthesis, leading to faster bone resorption and slower bone deposition). In conclusion, caffeine effectively increases PGE2 levels. PGE2 acts as a trigger for RANKL formation in osteoblasts and further increases the number of osteoclasts and orthodontic tooth movement (Herniyati *et al.,* 2018).

The effect of caffeine on OTM can also be seen from the activity of phosphodiesterases (PDE) which is known to increase levels of intracellular cyclic AMP (c-AMP) which serves to suppress bone resorption, as in the results of research conducted by Shirazi et al in 2017. Clinical findings by histological results show a decrease in the number of osteoclasts and root resorption. This caffeine has been shown to block adenosine receptors, inhibit PDE and counteract the effects of prostaglandins. In addition to exhibiting anti-inflammatory characteristics Adenosine, extracellular purines, exert their effects through cell surface receptors, which are widely distributed in various tissues, including bone.[11]

The OTM process can also be seen from bone remodeling, one indicator of which is ALP. In 2021, Arianda et al. conducted a study to look at the amount of *alkaline phosphatase (*ALP), ALP is a marker of osteoblast activity during new bone formation. ALP levels indicate biochemical changes that occur in the supporting tissue after application of orthodontic forces. This study said that the use of caffeine 2.7 mg can decrease ALP activity in alveolar bones. ALP levels in the treatment group that received cocoa drinks were lower than in the control group. Alveolar bone remodeling is also associated with observable changes in ALP activity from the GCF, an increase in high ALP levels signifies that osteoblast activity is increased. Increased osteoblast activity and ALP levels also indicate the formation of new bone. In this study it is said that if the formation of ALP goes down then the formation of new bone jg goes down on the compressive side. Cocoa containing caffeine can inhibit osteoblast activity by lowering ALP levels and the number of osteoblasts, thus potentially accelerating the movement of orthodontic teeth (Arianda *et al*., 2021).

However, Arnanda *et al*., 2020 study had different results, where the decrease in the mineral density of the right lower jaw alveolar bone showed no significant difference so it can be concluded that caffeine consumption in chocolate does not reduce the bone mineral density of the lower jaw alveolar bone in guinea pigs (*Cavia cobaya*) with the movement of orthodontic teeth. This is due to the presence of a number of confounding factors, including dosage differences where the effect or potency of caffeine on the body is proportional to the weight and height of the subject, meaning that the greater the body weight, the dose of caffeine needs to be increased, the duration of consumption, the method of administration and type, and the age range of the experimental animals used (Arnanda *et al*., 2020).

Those who play a role in the bone remodeling process are ALP and OPG (Arianda *et al*., 2021; Alhasyimi *et al*., 2019). ALP is a marker of osteoblast activity during new bone formation. Alveolar bone remodeling is also associated with changes in ALP activity in the GCF, an increase in high ALP levels signaling that osteoblast activity is increased. If the ALP goes down then new bone formation also goes down on the compressive side (Arianda *et al*., 2021). OPG is a natural receptor expressed by osteoblasts, OPG inhibits osteoclast differentiation and activity by binding to RANKL and blocking RANKL from interacting with RANK (Alhasyimi *et al*., 2019).

Those who play a role in the resorption process are RANKL, RUNX2, PGE2 (Alhasyimi *et al*., 2019; Alhasyimi *et al*., 2022; Herniyati *et al.,* 2018). The formation and activation of osteoclasts is regulated by RANKL. RANKL will accelerate tooth movement by promoting RANKL expression and increasing osteoclastogenesis. Conversely, increased levels of osteoprotegerin (OPG) produced by osteoblasts cause a decrease in RANKL levels and inhibit tooth movement (Alhasyimi *et al*., 2019). While changes in RUNX2 expression result in periodontal tissue reconstruction and tooth position shift. According to the findings, RUNX2 stimulates osteoclastogenesis and bone resorption via the AKT/NFATc1/CTSK axis. RUNX2 can also

trigger the expression of bone matrix genes, including osteocalcin and alkaline phosphatase, in the early stages of OTM (Alhasyimi *et al*., 2022). Next, PGE2 levels in the compression region were significantly greater than in the tensile region. Prostaglandins are involved in signal transduction. The mechanical deformation that occurs in the cells of the periodontal ligament will cause the release of the first messenger, including prostaglandins, the first messenger will then stimulate the release of the second messenger, including cAMP and intracellular calcium, which will then activate osteoclasts (Herniyati *et al.,* 2018).

CONCLUSION

The results of this study prove that cocoa administration contributes to active orthodontic treatment by modulating the rate of tooth movement, inducing osteoclastogenesis, and ultimately shortening the duration of orthodontic treatment. Based on several research journals, those that play a role in bone remodeling are ALP and OPG. The level must be low to speed up OTM. While those who play a role in bone resorption are RANKL, RUNX2, PGE2 so these levels must be high to accelerate OTM. Further studies are needed at the clinical level to confirm the efficacy and potential of cocoa in accelerating tooth movement in orthodontic patients (Alhasyimi *et al*., 2019).

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