**Moestopo International Review on Societies, Humanities, and Sciences (MIRSHuS)**
Vol. 5, No. 2 (2025) pp. 294-301
ISSN: 2775-9601

# TOXICITY TEST OF ROSELLE CALYX EXTRACT ON OSTEOBLASTS CELLS USING MTT ASSAY

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**ARTICLE INFO**
**Article History:**
received: 05/03/2024
revised: 11/09/2025
accepted: 04/10/2025

**Keywords:**
Roselle Extract; Osteoblast; MTT Assay

**DOI:**
10.32509/mirshus.v5i2.112

**ABSTRACT**
Background: Roselle calyx are the part of the roselle plant that is most often used as an extract because it has a lot of bioactive content. Roselle calyx contain dietary fiber, polyphenols, vitamin C, iron, zinc, calcium, magnesium, and potassium, often used as raw materials for herbal medicines. Polyphenols as a whole also have benefits for bone remodeling. Polyphenols can maintain bone integrity by reducing oxidative stress, reducing inflammation through signaling pro-inflammatory and modulation of osteoblastogenesis or osteoclastogenesis through osteoimmunological actions. Methods: Cytotoxicity was evaluated using MTT assay, and data were analyzed using the Shapiro-Wilk normality followed by one-way ANOVA and Tukey's HSD post hoc test. Results: The result showed that osteoblast cell viability after treatment with roselle calyx extract was 93.95% at 15%, 99.60% at 20%, 108.87% at 25%, and a concentration of 30% had the highest cell viability percentage of 136.69%. Conclusion: Roselle calyx extract is non-toxic to osteoblast cells and has the potential as an alternative natural material to inhibit relapse in orthodontic treatment.

## INTRODUCTION

Orthodontic treatment aims to achieve optimal tooth positioning both for aesthetic and functional purposes. Once the treatment is completed, it is crucial to maintain the new position of the teeth to ensure the long-term success of the treatment goals. However, the greatest challenge following orthodontic treatment is the tendency for teeth to revert to their original positions, leading to the loss of the corrections that have been made. Post-treatment relapse therefore not only undermines the aesthetic and functional outcomes but may increase the need for retreatment or extended retention phases. Orthodontic relapse may also lead to patient dissatisfaction, added financial burden, and extended retention phases, making its prevention a critical focus in contemporary orthodontics.

Orthodontic relapse is fundamentally a bone-biology problem. When teeth are moved, the periodontal ligament (PDL) and surrounding alveolar bone undergo remodeling through a tightly regulated balance of osteoclast-mediated resorption and osteoblast-mediated bone deposition (Krishnan & Davidovitch, 2006). Osteoblasts are responsible for synthesizing new bone matrix and promoting mineralization on the tension side of a moved tooth, thereby stabilizing its new position. If osteoblast

recruitment, proliferation, or activity is insufficient, newly formed bone may be inadequate, and the PDL fibers can contract, pulling the tooth back toward its original position. Thus, maintaining robust osteoblast function is essential to achieving long-term stability after orthodontic treatment (Tsolakis et al., 2023).

The common method used to prevent relapse in orthodontic treatment is the use of retainers. Various studies have been conducted to examine ways to prevent relapse. Currently, new materials for relapse prevention are being developed for direct application to the supporting tissues of the teeth. Research by Hadi et al. has demonstrated that injecting a hydrogel containing carbonated hydroxyapatite and chitosan into the gingival sulcus of incisor teeth in rats results in an increase in osteoblasts, which is a bone-forming cells, a decrease in osteoclasts, which is a bone-resorbing cells, and an increase in fibroblasts during the movement period associated with relapse (Hadi et al., 2024). These findings highlight increasing interest in biomolecular approaches that enhance alveolar bone remodeling to stabilize tooth position beyond mechanical retention alone.

Roselle is one of the herbal plants that is often used because it has various contents that are beneficial for body health. Roselle has properties as a digestive, anticancer, anti-inflammatory, antihypertensive, antidiabetic, antiplasmodic, antibacterial, antifungal, antihelmintic, antidiarrheal, hepatoprotective, diuretic, and as an antioxidant (Komala & Rosyanti, 2013; Li et al., 2022; Mahadevan et al., 2009; Mumpuni et al., 2021; Nurnasari & Khuluq, 2018; Riaz & Chopra, 2018). Roselle calyx are the part of the roselle plant that is most often used as an extract because it has a lot of bioactive content. Roselle calyx contain dietary fiber, polyphenols, vitamin C, iron, zinc, calcium, magnesium, and potassium, often used as raw materials for herbal medicines (Mariod et al., 2021; Osei-Kwarteng et al., 2021; Prasetyoputri et al., 2021). Polyphenols found in roselle play an essential role in bone remodeling by exerting antioxidative and anti-inflammatory actions on bone remodelling. Polyphenols have also been reported to modulate osteoblastogenesis and osteoclastogenesis through osteoimmunological regulatory pathways, ultimately supporting bone homeostasis (Nicolin et al., 2019). Therefore, roselle calyx extract has emerged as a promising candidate for natural therapeutic agents targeting bone-related conditions, including those associated with orthodontic treatment.

Before a biomaterial or plant extract can be applied in proximity to bone cells in the oral environment, its cytocompatibility must be rigorously evaluated. The MTT assay is one of the most widely accepted in vitro methods to determine cell viability because it quantitatively measures mitochondrial metabolic activity (Mosmann, 1983). Living cells contain active mitochondrial dehydrogenase enzymes that convert MTT reagent into purple formazan crystals (Fotakis & Timbrell, 2006). The amount of formazan produced is directly proportional to the number of viable cells, allowing precise and reproducible assessment of cytotoxicity.

Based on previous findings supporting the role of roselle calyx extract in enhancing bone healing processes, this preliminary study was designed to evaluate the cytocompatibility and potential of ethanol extract of roselle calyx as a novel therapeutic agent for preventing post-orthodontic relapse through improved alveolar bone stability.

## METHODS

### Extraction of Roselle Calyx

Roselle calyx dried with oven at a temperature of 50°C for 24 hours until it is marked as easily crushed when squeezed. Dried roselle calyx are crushed with a blender until smooth. Then sifted using a 60 mesh sieve. The making of roselle calyx extract is done by maceration, namely with Weigh 2 kg of powder roselle calyx and put into a pumpkin Erlenmeyer. Add 96% ethanol solvent in the ratio powder to ethanol is 1:4. Then macerated for 2 hours at a temperature of 60 °C ±2 °C. The solution is filtered using a normal cloth filter

to remove large-sized dregs. The Roselle extract is then filtered with Whatman paper No. 1 and concentrated using a vacuum rotary evaporator.a temperature of 50°C and a pressure of 100mbar. The termination of the evaporation process is determined by no dripping solvent until the obtained extract thick of roselle calyx.

**Test Cytotoxicity**

This cytotoxicity was carried out using the MTT Assay test method. The cytotoxicity test was conducted using roselle calyx extract at concentrations of 15%, 20%, 25%, and 30%. The control group consisted of untreated osteoblast cells cultured in complete Dulbecco's Modified Eagle Medium (DMEM) without extract application. Each treatment and control group was tested in five technical replicates (n = 5) per concentration, as presented in Table 4.1 within a single biological experiment. Sample size selection followed the standard practice for MTT-based cytotoxicity studies, which typically use three to five replicates to achieve acceptable statistical reliability and variance control (Almutary & Sanderson, 2016; Min Seung et al., 2021). Quality assurance was maintained by using cells from the same passage, identical culture conditions, and consistent reagent batches. The mean optical density (OD) values and standard deviations were used to verify data consistency before analysis.

Preparation of cell culture osteoblasts done in laminar flow. MTT testing uses cell osteoblasts in monolayer form with Eagle's media and 5% Fetal Bovine Serum (FBS) was planted in roux culture bottle which are then treated in incubation at 37°C for 48 hours. Osteoblasts cells from human dental pulp stem cells (hDPSCs) obtained from PT Prodia Stem Cell, Indonesia. Cytotoxicity test was performed by the 3-(4,5- dimethyl-2-thiazolyl)-2.5- diphenyltetrazoliumbromide (MTT) assay. Yellow water-soluble MTT is metabolically reduced in viable cells to a blue-violet insoluble formazan. The cell viability information was known by the change of formazan salt due to mitochondrial activation of living cells. An enzyme-linked immunosorbent assay reader was used to analyze the optical density of the formazan salt. A decrease in the number of living cells resulted in a decrease in the metabolic activity of the cell, and this was monitored by the optical density at 570 nm. The cell viability ratio was determined to be the ratio between the absorbance of the tested well and the absorbance of the control well by using the following equation. The percentage of cell viability and inhibition is calculated using the following equation (Kamiloglu et al., 2020):

$$\% \text{ Viability} = \frac{\text{Mean OD of sample}}{\text{Mean OD of blank}} \, x \, 100$$

**Data Analysis**

Data analysis is preceded with normality test using the Shapiro-Wilk test. For see there is or whether or not difference is meaningful in a way, statistics between group One Way ANOVA test is carried out if normal data distribution or Kruskal Wallis Test if data distribution is not normal.

## RESULTS

The results of absorbance readings using ELISA reader on osteoblast cell plates are presented in table 4.1 which shows the results of MTT assay testing on osteoblast cells with various concentrations. From the absorbance results, cell viability was then calculated and the results obtained at a concentration of 15% had the lowest cell viability percentage of 93.95%, a concentration of 20% had a cell viability percentage of 99.60%, a concentration of 25% had a cell viability percentage of 108.87% and a concentration of 30% had the highest cell viability percentage of 136.69%.

**Table 4.1** Results of MTT- assay Testing on Osteoblast Cells After 48 Hours of Incubation with 5 Repetitions.

| Group | 1 | 2 | 3 | 4 | 5 | Average |
|---|---|---|---|---|---|---|
| Roselle Extract 15% | 0.241 | 0.234 | 0.234 | 0.225 | 0.233 | 0.233 |
| Roselle Extract 20% | 0.241 | 0.254 | 0.245 | 0.247 | 0.249 | 0.247 |
| Roselle Extract 25% | 0.251 | 0.281 | 0.276 | 0.277 | 0.265 | 0.270 |
| Roselle Extract 30% | 0.351 | 0.357 | 0.359 | 0.303 | 0.327 | 0.339 |
| Cell + DMEM | 0.244 | 0.271 | 0.231 | 0.246 | 0.247 | 0.248 |

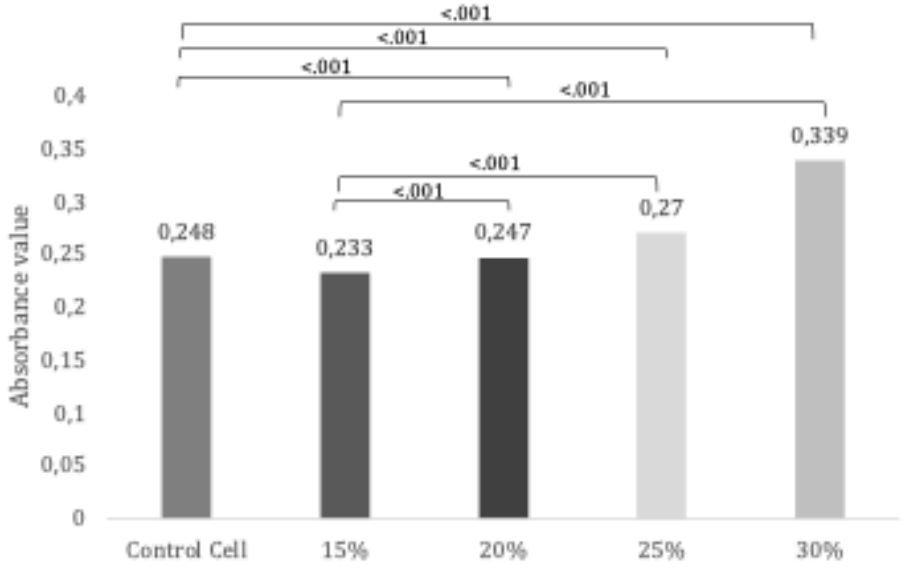


**Figure 4.1** The absorbance value between concentrations of roselle calyx extract.

**Discussion**

The results of the study showed that the concentration of roselle calyx extract of 15% had the lowest percentage of cell viability of 93.95%, the concentration of 20% obtained a percentage of cell viability of 99.60%, the concentration of 25% obtained a cell viability percentage of 108.87%, and a concentration of 30% has the highest cell viability percentage of 136.69%. Based on the results of the cell viability percentage test, all samples were > 50% and declared non-toxic. This is supported by the in vivo acute toxicity test conducted by Sari et al., stated that roselle calyx extract did not cause any toxic effects and there were no delayed toxic effects for 14 days in Sprague dawley rats (Sari et al., 2016).

The viability of osteoblast cells increases with increasing concentration of roselle calyx extract, which is also proven by the highest percentage of cell viability at a concentration of 30% roselle calyx extract. This is because roselle calyx contains flavonoids, saponins, phenolics, tannins, and quercetin (Kusparmanto et al., 2024; Obouayeba et al., 2014; Suniarti et al., 2022). Flavonoid content can prevent inflammation by increasing osteoblast function. Flavonoids have bone anabolic activity that has more effects than inhibiting bone resorption through suppressing osteoclast activation (Cao et al., 2022; Weaver et al., 2012).

Flavonoid can increase the process of osteoblast differentiation into osteocytes in the osteogenesis process. Bone formation occurs by stimulating osteoblast differentiation and cell proliferation by inhibiting adipogenesis through the nitric oxide and estrogen receptor pathways (Sharma et al., 2023).This study tested the potential of roselle calyx extract on osteoblast cell viability as an effort to support the bone remodeling in the prevention of relapse post orthodontic treatment. Flavonoids in roselle

calyx extract have strong antioxidant activity, which can help reduce oxidative stress in bone tissue and support the bone remodeling (Sura et al., 2018). This mechanism has been demonstrated in numerous studies showing that flavonoids enhance alkaline phosphatase (ALP) expression, Runx2 signaling, and calcium deposition, which are hallmarks of osteoblast maturation (Ramesh et al., 2021).

The increase in osteoblast viability observed in this study suggests that roselle calyx extract provides a favorable microenvironment for bone cell health and metabolic activity. Therefore, the progressive increase in cell viability from 15% to 30% concentrations indicates a dose-dependent positive effect of roselle bioactive compounds on osteoblast biological function. When osteoblast activity is optimal, newly remodeled alveolar bone can better resist the elastic recoil of periodontal fibers following appliance removal, ultimately reducing relapse (Krishnan & Davidovitch, 2006).

The MTT assay provided a quantitative evaluation of mitochondrial activity, and the increased formazan production at higher concentrations of extract suggests enhanced cellular respiration and metabolic performance (Fotakis & Timbrell, 2006; Mosmann, 1983). Therefore, roselle extract may not only preserve cell survival but also stimulate active cellular processes linked to bone regeneration. These biological benefits are particularly relevant for orthodontics, where long-term stabilization depends on strong alveolar bone support following tooth movement (Proffit et al., 2019). During orthodontic relapse, bone resorption occurs more rapidly than bone deposition, and the PDL fibers contribute elastic forces that displace teeth back toward their original positions (Meeran, 2012).

The use of roselle extract in the oral cavity also aligns with current trends toward biocompatible, plant-based biomaterials in dental research (Ikbal et al., 2025). Unlike synthetic chemical agents, roselle extract may offer a safer and more holistic approach by supporting tissue regeneration while minimizing risk of toxicity. Additionally, polyphenols in roselle calyx extract have demonstrated antimicrobial effects that may protect periodontal tissues from pathogenic invasion during orthodontic post-treatment phases (Jabeur et al., 2017). Healthy gingival tissues and PDL support are critical components in preventing unwanted tooth migration.

## CONCLUSION

This study investigated the toxicity profile of roselle (*Hibiscus sabdariffa* L.) calyx extract on osteoblast cells using the MTT assay to assess its biocompatibility for orthodontic relapse prevention. The results demonstrated that treatment with roselle extract maintained high cell viability across all tested concentrations. Specifically, osteoblast viability was 93.95% at 15%, 99.60% at 20%, 108.87% at 25%, and reached its highest value of 136.69% at a concentration of 30%. These findings indicate that roselle calyx extract not only meets the >50% viability threshold for non-cytotoxicity but also enhances metabolic activity and promotes osteoblast cell proliferation at higher concentrations.

The cytocompatibility observed suggests that the bioactive components found in roselle, such as flavonoids and phenolic compounds, may support cellular responses beneficial for bone remodeling. Although promising, these results represent an initial in vitro assessment conducted from a single biological experiment with limited replicates. Further investigations, including studies with multiple independent repeats, molecular mechanism analysis, optimal dosing evaluation, and in vivo validation, are required to ensure safety and confirm therapeutic efficacy.

Overall, roselle calyx extract demonstrates favorable compatibility with osteoblasts and has potential for future development as a natural biomaterial candidate, particularly in applications for orthodontic relapse prevention.

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