The Effect Of Mangosteen Pericarp (Garcinia Mangostana L.) Extract Mucoadhesive Gingival Patch On The Mda Levels And The Number Of Micronuclei Due To Panoramic Radiography Radiation

by Eha Astuti

Submission date: 11-Dec-2020 10:02AM (UTC+0800)
Submission ID: 1471599003
File name: The_Effect_Of_Mangosteen_Pericarp_Garcinia_Mangostana_L..pdf (90.98K)
Word count: 4412
Character count: 22922

DocID: https://connectjournals.com/03896.2020.20.4877

Biochem. Cell. Arch. Vol. 20, No. 2, pp. 4877-4882, 2020 | www.connectjournals.com/bca | *ISSN 0972-5075*

THE EFFECT OF MANGOSTEEN PERICARP (*GARCINIA MANGOSTANA* L.) EXTRACT MUCOADHESIVE GINGIVAL PATCH ON THE MDA LEVELS AND THE NUMBER OF MICRONUCLEI DUE TO PANORAMIC RADIOGRAPHY RADIATION

Deny Saputra[1]*, Eha Renwi Astuti[1], Anindita Daraninggar[2], Anisah Rachmatul Alam[2], Febrianti Adi Satria[2] and Muhammad Aulia[2]

[1]Department of Dentomaxillofacial Radiology, Faculty of Dental Medicine, Universitas Airlangga, Surabaya, Indonesia.
[2]Undergraduate Student, Faculty of Dental Medicine, Universitas Airlangga, Surabaya, Indonesia.
*e-mail: deny-s@fkg.unair.ac.id

(Received 18 July 2020, Revised 12 September 2020, Accepted 26 September 2020)

ABSTRACT : The aim of this study is to determine the effect of mangosteen pericarp mucoadhesive gingival patch on the MDA levels and the number of micronuclei in gingival tissues due to panoramic radiography radiation. 35 *Rattus norvegicus* samples were divided into 7 groups and were given mucoadhesive gingival patches. Then, the rats were exposed to x-ray radiation. The gingival tissues were taken for histopathological examination to determine the micronuclei number and TBARS Test for the MDA levels. There were differences in MDA levels and micronuclei number between rats treated with mangosteen gingival patches and those did not. Application of mangosteen pericarp mucoadhesive patches can reduce the MDA levels and the number of micronuclei in rat's gingival tissues due to panoramic radiography radiation.

Key words : Herbal medicine, malondialdehyde, micronuclei, mucoadhesive gingival patch, *Garcinia mangostana* L.

INTRODUCTION

Radiographic examination is an important examination to support the diagnosis and appropriate treatment, especially in the field of dentistry (Gupta *et al*, 2014). Panoramic radiography is a low-dose x-ray radiography technique, which has a dose of 9-14 µSv (White and Pharoah, 2014). Although, it is low-dose radiation, the use of ionizing radiation still has a negative effect on human cells cannot be fully protected from the effects of radiation (Zhang *et al*, 2014; Yusuf *et al*, 2018). Panoramic radiography produces ionizing radiation, which can cause the formation of free radicals in the exposed area. Free radicals have very reactive properties and can cause changes to important molecules in cells, especially DNA (Hasan and Djakaria, 2013).

X-ray radiation produces free radical products in the form of ROS (Reactive Oxygen Species), which can trigger oxidative stress and cause cell damage and death (Kumar *et al*, 2012). Oxidative stress is an imbalance ratio between free radicals and antioxidants. Oxidative stress can cause damage to DNA, RNA, protein and lipids. ROS will react with unsaturated lipids in cell membranes and plasma and cause the formation of lipid peroxide or MDA (Malondialdehyde) (Freitinger *et al*, 2012; Narmada *et al*, 2020).

ROS that binds to unsaturated fat molecules or PUFA (Poly Unsaturated Fatty Acid) will initiate the lipid peroxidation process. This is a process of oxidative damage to unsaturated fatty acids that can produce secondary products in the form of MDA compounds (malondialdehyde), which are 3-carbon low molecular weight and are often used as lipid peroxidation markers. Increased levels of MDA can be interpreted as an increase in the number of free radicals in the body (Spirlandeli *et al*, 2014; Aulia *et al*, 2017; Nugraha *et al*, 2020).

The formation of free radicals due to X-ray exposure can trigger oxidative stress. This can cause DNA damage due to nucleus anomalies that cause the formation of micronuclei (Xotlanihua-Gervacio *et al*, 2018). Micronuclei are often used as biomarkers of chromosomal damage that contribute to carcinogenesis (Kesidi *et al*, 2017) and an increased number of micronuclei demonstrates the increased frequency of chromosomal damage and changes in cell nuclei (Shantiningsih and Diba, 2015). Micronuclei are extra-small nuclei formations

separated from the nucleus. Micronuclei are formed due to chromosome fragmentation in the nucleus at the anaphase stage during the process of cell mitosis (Luzhna *et al*, 2013).

The human body can suppress the number of free radicals in the presence of antioxidants. Various studies have demonstrated that mangosteen peel has several benefits such as antioxidants, anti-tumor, anti-allergic, anti-inflammatory, anti-bacterial, anti-diabetes and anti-viral (Ighodaro and Akinloye, 2018; Ansori *et al*, 2020). Mangosteen rind contains high levels of complex antioxidants, especially phenolic compounds or polyphenols, including xanthones and epicatechins (Yu *et al*, 2007). The xanthone bioactive substance contained in mangosteen peel extract has the ability to control the production of cisplatin as a second line antioxidant defense, inhibiting the chain initiation or breaking the free radical chain propagation reaction (EL-Meghawry EL-Kenawy *et al*, 2019).

This study used mangosteen peel extract in a paste preparation applied in the form of a mucoadhesive gingival patch. Along with the development of pharmaceutical technology, the use of drugs in the mucosal area has developed into mucoadhesive drugs, which is a system designed to attach to the mucosal layer and has the ability to extend the contact time of drugs at the application site (Shan *et al*, 2011). Patch-shaped drug preparations have various advantages such as flexible, fast start, easier use and storage and better accuracy in comparison to other preparations such as syrup (Silva *et al*, 2015). This motivates the authors to study the effect of mangosteen gingival patch (*Garcinia mangostana* L.) on MDA levels and the number of gingival tissue micronuclei in rats (*Rattus norvegicus*) due to exposure to panoramic radiographic radiation.

MATERIALS AND METHODS

This research was an experimental laboratory analytic study with a randomized post-test only control group design. The samples of this study were rats (*Rattus norvegicus*) weighted 200–250 grams, male, at least 3 months old and in good health. The 35 samples of *Rattus norvegicus* were then divided into 7 with 5 rats per group. The study was conducted after obtaining a certificate of Ethical Clearance (number: 354 / HRECC.FODM / VI / 2019) issued by the Health Research Ethical Clearance Commission, Faculty of Dentistry, Airlangga University.

Production mangosteen skin extract

Mangosteen peels were cut into small pieces and dried for 1 day. The dried peels were then blended and sieved to obtain a yellowish-brown powder. 250 gr mangosteen peel powder was macerated using 96% ethanol as much as 1000 ml for 2 days and then filtered with filter paper so as to obtain as much as 600 ml of liquid. The liquid was evaporated with a Rotary Vacuum Evaporator at 40°C. The final product was mangosteen peel paste (Loegito, 2018).

Making the patch gingival mucoadhesive mangosteen peel extract is made using a solvent casting technique

Stage 1 : A total of 1.5 grams of CMC-Na was dissolved in 30 mL distilled water and allowed to stand for 15 minutes. The mixture was then crushed using a mortar and stampler to form a gel mass and add 60.3 g of hot distilled water little by little to the gel base. Stage II: Dissolve 0.5 grams menthol with enough ethanol and mix with 0.5 grams of mangosteen peel extract until homogeneous. Add 2.5 grams of propylene glycol to the solution until homogeneous. The stage I formula was mixed in the stage II formula and stirred until homogeneously weighed 70gr for stage III preparations into a petri dish and dried in an oven at 45°. Patch resulting in a gel preparation with elastic properties, not easily torn, did not affect the results of radiographic examination (Tiensi *et al*, 2018).

Application of mangosteen patch in experimental animals

The gingival patch was applied in all parts of the maxillary and mandibular of anesthetized rats. The anesthesia involved 0.2 cc for ± 60 minutes. The patches were cut into small pieces and adjusted to the size of the gingival mucosa in the rats' jaw. The patch was applied by opening the rat's jaw using a needle holder and positioned using dental tweezers.

X-Ray irradiation

Radiation exposure was carried out using Asahi Hyper-X CM digital panoramic dental radiography (power supply 220V; 1.2; 1.5 kVA; 50/60 Hz). Anesthetized Rattus norvegicus were arranged in such a way on a wooden board with a height parallel to the chinrest panoramic radiographic machine (Pramitasari, 2014).

The research group

The research group was divided based on the presence or absence of patches and panoramic radiation. There were 7 groups. The positive control group (KP) was not irradiated and not treated, negative control group 1 (KN1) was irradiated, not treated and observed on day 1, negative control group 2 (KN2) was irradiated, not treated, and observed on day 5, negative control group 3 (KN3) was irradiated, not treated and observed on day

7, treatment group 1 (P1) was irradiated, treated, and observed on day 1, treatment group 2 (P2) was irradiated, treated, and observed on day 5 and treatment group 3 (P3) was irradiated, treated and observed on day 7.

Retrieval of animal tissue

Retrieval of the tissue began with ketamine anesthesia at lethal doses. Half of the maxilla and mandible were then retrieved. The retrieved tissue was stored in a physiological NaCl solution for MDA samples and in 10% formalin for 24 hours for micronuclei samples.

Gingival tissue sample processing for MDA observation

A total of 0.5 grams of gingival tissue, was mixed in quartz sand and added 2 ml of 1.15% KCl then crushed using a mortar until smooth. Insert the softened tissue into a polypropylene tube and then add 3 ml of 20% Acetic Acid and 0.4 ml of SDS 8.1%. Add 3 ml of 1% Thiobarbituric Acid (TBA) and 0.5 ml of HCl 0.1 N, then homogenize using a vortex mixer. The mixture was centrifuged at 3000 rpm for 1 minute. The mixture was heated in a 100°C water bath for 135 minutes and cooled at room temperature (Shaikh *et al*, 2011).

Processing samples of gingival tissue for micronuclear observation

Began with ketamine anesthesia at lethal doses. Half of the mandibles were then taken. The mandible was fixed in 10% formalin for 24 hours. Then, the mandible was transferred to decalcification fluid (pure EDTA) until the bone has softened (30 days) and ready for the tissue cutting stage. Once the mandible is soft, the best one was then chosen according to the location for examination. The tissue was cut into approximately 2–3 mm thickness and put into tapes and coded according to the group. The tissue was then processed with the Automatic Tissue Tex Processor for 90 minutes. The tissue was then removed from the device and blocked with paraffin per tissue code, cut with a microtome with a thickness of 3–5 microns, placed in an oven for 30 minutes at 70–800°C, put into 2 tubes of xylol solution for 20 minutes each, put into four alcoholic tubes (99%, 95%, 90%, 70%) for 3 minutes each (Hydration) and the last, put in running water for 15 minutes. To make preparations by painting HE (Hematoxylin Eosin), the solution was Mayer Hematoxylin carried out for 10 minutes then rinsed with water. Painting with eosin solution for 30 seconds, then washed with 70% alcohol, 80%, 90% 95%, 99% each for 2 minutes and then given xylol for 4 minutes. Then the mounting process by means of the preparation is closed with a glass covered balsam canada or entelen (Indrawati, 2017).

MDA level measurement

Color changes that occur in the solution were observed using a spectrophotometer at a wavelength of 532 nm and the MDA levels were calculated using a regression line from the standard curve of solution 1.1.3.3 tetrameter propane.

Measurement of the number of micronuclei

Was done by observing the anatomic histopathological preparations that have been stained HE under a light microscope at 400x magnification. The number of micronuclei was determined by calculating the number of micronuclei visible on the 5 field of view.

RESULTS

The effect of mangosteen peel gingival patch (*Garcinia mangostana* L.) on malondialdehyde (MDA) levels was examined using a T-BARS test and then averaged. Measurement of the number of micronuclei was performed by observing the anatomic histopathological preparations by staining HE (Haematoxylin Eosin). Mangosteen peel extract used has been tested High Performances Liquid Chromatography (HPLC) using a standard curve dissolved in ethanol to determine the á-mangosteen content and obtained a result of 1.128%. The average number of MDA levels and micronuclei are presented in Table 1. Results of the Kruskal-Wallis of MDA levels and the number of micronuclei among the study groups are presented in Table 2.

Table 1 : Average results of MDA test levels and average number of micronuclei.

No	Groups	MDA Levels	Micronuclei
1	Positive control groups (KP)	0.23135822	0.44
2	Negative control groups 1 (KN1)	0.24358264	1.76
3	Negative control groups 2 (KN2)	0.2681765	4.92
4	Negative control groups 3 (KN3)	0.2833073	5.24
5	Treatment group 1 (P1)	0.14507812	1.76
6	Treatment group 2 (P2)	0.14469236	1.87
7	Treatment group 3 (P3)	0.2147984	3.35

Table 2 : Results of the Kruskal-Wallis of MDA levels and the number of micronuclei among the study groups.

Statistic Test	Groups	Asym. Sig
Kruskal-Wallis	MDA	0.245
One-way Anova	Mikronuklei	0.014

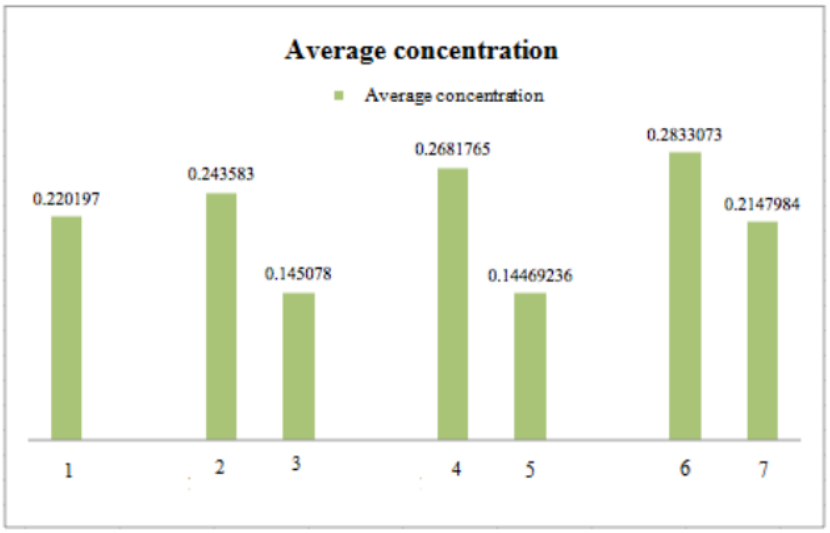

Fig. 1 : Graph of average MDA levels between groups.

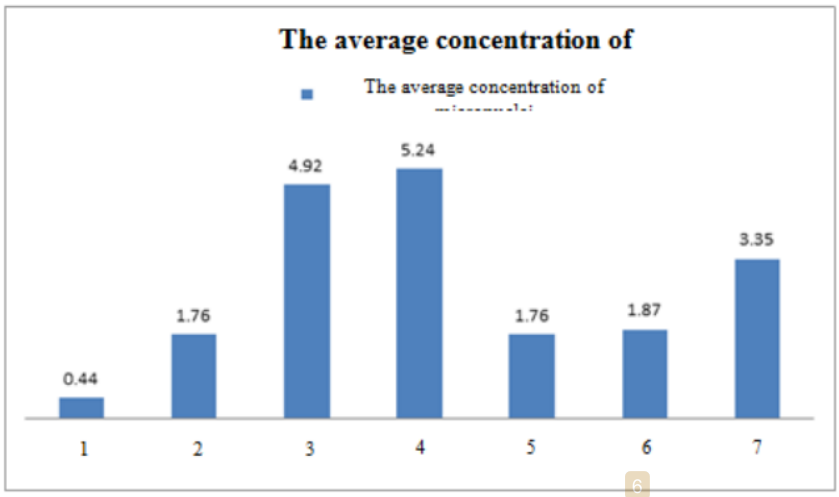

Fig. 2 : Graph of the average number of micronuclei between positive control groups, negative control 1, negative control 2, negative control 3, treatment 1, treatment 2, and treatment 3.

Fig. 1 shows that irradiation can increase MDA levels on irradiated gingival tissue compared to non-irradiated samples. The graph shows that the patch reduced the MDA levels that untreated samples demonstrated higher MDA levels.

Fig. 2 shows that MDA levels found highest in negative control group 3 and found lowest at positive control groups.

DISCUSSION

Panoramic radiography produces ionizing radiation that can initiate free radical formation in the exposed area and cause changes to important molecules in cells, especially DNA (Hasan and Djakaria, 2013). Free radicals can also cause peroxidation processes that produce MDA, which is a marker of free radical activity in the body. Increased levels of MDA can be interpreted as an increase in the number of free radicals in the body (Spirlandeli *et al*, 2014; Aulia *et al*, 2017). This study found insignificant differences of MDA levels for samples treated with a gingival patch containing mangosteen peel. The results were insignificant in data analysis (Table 1) and statistical analysis (Table 2). Table 2 shows an increased mean of micronuclei between the positive control group and the negative group, and there were significant differences based on statistics ($p < 0.05$). There was an increase in the mean micronuclei in negative control groups on day 1, 5 and 7.

Increased levels of MDA and micronuclei are consistent with the theory, stating that panoramic

radiographic radiation exposure has a biological effect in the form of cell damage through oxidation reactions that produce free radicals which trigger lipid peroxidation and micronuclei formation. Sheikh *et al* (2012) on the genotoxic effects of panoramic radiographic irradiation in gingival epithelial cells found a significant increase of micronuclei in gingival epithelial cells before and after exposure (Sheikh *et al*, 2012).

The mean of MDA levels in the treatment groups was lower than the non-treated groups. This was because the mucoadhesive gingival patch tract contains xanthone, which has an antioxidant property (Gutierrez-Orozco and Failla, 2013). Derivate xanthone, á-mangostin acts as an antioxidant that can reduce MDA levels, and it works by eliminating ROS; therefore, preventing lipid peroxidation and reducing MDA levels and ROS formed during oxidative stress processes (Patil and Masand, 2019). We also use ethanol on dried mangosteen peel extract to maximize the antioxidant property.

The average number of micronuclei between groups observed on day 1 was the same. This was possibly due to the mitosis process that micronuclei formation could not be observed histopathologically. On observation day 5 and 7, the average number of micronuclei of the treatment group was not significantly lower than the non-treatment ($p > 0.05$).

Radiation-induced tissue changes depend on the dose and duration of radiation (Dungir *et al*, 2012). This study utilized digital panoramic radiography, which produces a lower radiation effect compared to conventional panoramic radiography. The panoramic radiography was the Asahi Hyper X panoramic, which was according to Matsuda *et al* (2009), has a parameter of 12.76 µSv, whereas conventional panoramic according to Mettler *et al* (2008) has a parameter of 0.1 (0.03-0.22) mSv. This confirms that the digital panoramic radiography used in the study had a very low radiation dose that could not cause significant cell changes.

Another factor that might influence was the level of radiosensitivity of the tissue, which was relatively low (Saputra *et al*, 2012). Microscopic examination revealed that the gingival tissue consists of layered squamous epithelium and the central core underlying connective tissue (Okano and Sur, 2010). Squamous epithelial cells have a low level of radiosensitivity compared to other cells such as basal cells found in the oral mucous membrane, and endothelial cells of the vascular system. Oral mucous membranes consist of a basal layer consisting of radiosensitive stem cells that are able to divide and replicate quickly. Radiosensitivity of a tissue or organ can be measured by its response to irradiation, one of which is cell death, which can be caused by the presence of free radicals in the body (Newman *et al*, 2019).

Another possibility was the duration of the gingival patches application. In this study, the timing of patch removal from the gingival tissue mucosa was uncertain. The patches removal was quite short considering rats' small mouth and possibly swallowed as the anesthetic effect ended in 30 minutes to 2 hours after injection. Another possible cause was that the patches did not use ethyl cellulose for backing layer to prevent the entry of saliva into the patch and cause a swelling process which can prolong the attachment of the patch and the diffusion process of active ingredients in the tissue so that the antioxidant content can work in a maximum level. Previous studies conducted by Shantiningsih in 2014 on gingival patch attached to the gingival mucosa New Zealand rabbit, which lasted up to 6 hours, showed a significant result (Shantiningsih and Diba, 2015).

CONCLUSION

Application of mangosteen pericarp mucoadhesive patches can reduce the MDA levels and the number of micronuclei in rats' gingival tissues due to panoramic radiography radiation.

REFERENCES

Ansori A N M, Susilo R J K, Fadholly, Hayaza S, Nugraha A P and Husen S A (2020) Antidiabetes type 2 phytomedicine: Mangosteen (*Garcinia mangostana* L.) - a Review. *Biochem. Cell. Arch.* **20**(Supplement 1), 3173-3177.

Aulia A N, Sunariani J and Rachmat E A (2017) Changes in taste sensation of sour, salty, sweet, bitter, umami and spicy, as well as levels of malondialdehyde serum in radiographers. *Dental J.* (Majalah Kedokteran Gigi). **49**, 2, 110-114. DOI: http://dx.doi.org /10.20473/j.djmkg.v49.i2.p110-114.

Dungir S G, Katja D G and Kamu V S (2012) Antioxide Activity of Phenolic Extract from Mangosteen Skin (*Garcinia mangostana* L.). *Jurnal MIPA* **1**(1), 11-15. DOI: https:// doi.org/10.35799/jm.1.1.2012.424

EL-Meghawry EL-Kenawy A, Hassan S M and Hussein Osman H E (2019) Mangosteen (*Garcinia mangostana* L.) Mangosteen fruit and its sources Nonvitamin and Nonmineral nutritional supplements. Elsevier Inc. doi: 10.1016/B978-0-12-812491-8.00045-X.

Freitinger S Z, Zolzer F, Berane L and Racek J (2012) Indicators of oxidative stress after ionizing and/or non-ionizing radiation: Superoxid dismutase and malondialdehyde. *J. Photochem. Photobiol. B: Biol.* **117**, 111–114. DOI: 10.1016/j.jphotobiol .2012.08.009

Gupta A, Devi P, Srivastava R and Jyoti B (2014) Intra oral periapical radiography. *Bangladesh J. Dental Res. & Educ.* **4**(2), 83–87. https://doi.org/10.3329/bjdre. v4i2.20255

Gutierrez-Orozco F and Failla M L (2013) Biological activities and

bioavailability of mangosteen xanthones: A critical review of the current evidence. *Nutrients* **5**(8), 3163–3183. doi: 10.3390/ nu5083163

Hasan I and Djakaria H M (2013) Cell Death due to Radiation. *J. Indonesian Radiation Oncology Society* **4**(2), 125-135. https:// doi.org/10.32532/jori.v4i2.14

Ighodaro O and Akinloye O (2018) First line defense antioxidants-superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX): Their fundamental role in the entire antioxidant defense grid. *Alexandria J. Med.* **54**(4), 287-293. https://doi.org/10.1016/j.ajme.2017.09.001

Indrawati A (2017) Teknik Pembuatan Dan Evaluasi Preparat Histologi Dengan Pewarnaan Hematoksilin Eosin Di Laboratorium Histologi Dan Biologi Sel Fakultas Kedokteran Ugm Dan *National Laboratory Animal Center* (NLAC) *Mahidol University*. Thesis. Universitas Gadjah Mada Yogyakarta.

Kesidi S, Maloth K, Reddy K and Geetha P (2017) Genotoxic and cytotoxic biomonitoring in patients exposed to full mouth radiographs – A radiological and cytological study. *J. Oral and Maxillofacial Radiology* **5**(1), 1-6. DOI: 10.4103/ jomr.jomr_47_16

Kumar V, Cotran R S and Robbins S L (2012) *Handbook of Pathology* **7th** Ed. Jakarta: EGC. pp. 4, 7-9, 27, 29-31.

Loegito M (2018) The Effects of Ethanol Extract of Mangosteen (*Garcinia mangostana* L.) Skin on Testicular Histopathological Structure, Levels of MDA and SOD of Epididymis Spermatozoa, and Mortality and Viability of Spermatozoa of Wistar Rats (*Rattus norvegicus*) Exposed to Cigarette Smoke. Dissertation. Universitas Brawijaya Malang. p.222-224.

Luzhna L, Kathiria P and Kovalchuk O (2013) Micronuclei in genotoxicity assessment: from genetics to epigenetics and beyond. *Frontiers in Genetics* **4**, 131. doi: 10.3389/ fgene.2013.00131

Matsuda T, Okano T, Endo A, Katoh T, Kaneko N and Harata Y (2009) An optically stimulated luminescence dosimeter to measure an organ dose in diagnostic radiology. In: Programme and Abstract Book, **17th** International Congress of Dentomaxillofacial Radiology. p.133

Metler F A, Huda W, Yoshizumi T T and Mahesh M (2008) Effective doses in radiology and diagnostic nuclear medicine: a catalog. *Radiology* **248**, 1, 254-63. doi: 10.1148/ radiol.2481071451.

Narmada I B, Sarasati A, Wicaksono S, Rezkita F, Wibawa K G P, Hayaza S and Nugraha A P (2020) Phytochemical Screening, Antioxidant Activity, Functional Groups and Chemical Element Characterization Analysis of (-)-Epigallocatechin-3-Gallate (EGCG) in East Javanese Green Tea Methanolic Extract: An Experimental In Vitro Study. *Sys Rev Pharm*. **11**(5), 511-519.

Newman M, Klokkevold P, Carranza F and Takei H (2019) Newman and Carranza's Clinical Periodontology. Philadelphia: Elsevier. 13th ed. p.189.

Nugraha A P, Narmada I B, Sitasari P I, Inayati F, Wira R and Triwardhani A (2020) High mobility group box 1 and heat shock protein-70 expression post (-)-epigallocatechin-3-gallate in East Java green tea methanolic extract administration during orthodontic tooth movement in wistar rats. *Pesqui Bras Odontopediatria Clín Integr*. **20**, e5347, 1-10

Okano T and Sur J (2010) Radiation dose and protection in dentistry. Japanese Dental Science Review. *Japanese Association for Dental Sci*. **46**, 2, 112–121. https://doi.org/10.1016/ j.jdsr.2009.11.004

Patil V M and Masand N (2019) Anticancer Potential of Flavonoids: Chemistry, Biological Activities and Future Perspectives. 1st ed, Studies in Natural Products Chemistry. **1st** ed. Elsevier B.V. p.278-289.

Pramitasari N P (2014) Effects of X-Ray Irradiation on Micronucleus Erythrocyte Polychromatic Rattus Norvegicus Male Wistar Strain (Laboratory Experimental Analytical Research). *Thesis*. Universitas Airlangga Surabaya.

Saputra D, Astuti E R and Budhy T I (2012) Apoptosis and necrotic oral mucosa cell induced by conventional dental x-ray radiation. *Dentomaxillofacial Radiol. Dental J*. **3**(1), 36– 40.

Shaikh R, Singh T, Garland M and Woolfson A (2011) Donnelly R. Mucoadhesive drug delivery systems. *J. Pharm. Bioall Sci*. **3**(1), 89-100. doi: 10.4103/0975-7406.76478

Shan T, Ma Q, Guo K, Liu J, Li W and Wang F (2011) Xanthones from mangosteen extracts as natural chemopreventive agents: potential anticancer drugs. *Curr. Mol. Med.* **11**(8), 666-77. doi: 10.2174/156652411797536679.

Shantiningsih R R and Diba S F (2015) Effect of β-carotene Gingival Mucoadhesive Patch Application at Panoramic Radiography Exposure. *Majalah Kedokteran Gigi Indonesia* **1**(2), 186-192. https://doi.org/10.22146/majkedgiind.9121

Sheikh S, Pallagatti S, Grewal H, Kalucha A and Kaur H (2012) Genotoxicity of digital panoramic radiography on oral epithelial tissues. *Quintessence Int.* **43**, 8, 719-25.

Silva B, Borges A, Silva C, Coelho J and Simões S (2015) Mucoadhesive oral films: The potential for unmet needs. *Int. J. Pharmaceutics* **494**(1), 540. doi: 10.1016/j.ijpharm.2015.08.038

Spirlandeli A L, Deminice R and Jordao A A (2014) Plasma Malondialdehyde as Biomarker of Lipid Peroxidation: Effects of Acute Exercise. *Int J Sports Med*. **35**(01), 14–18. DOI: 10.1055/ s-0033-1345132.

Tiensi A N, Ratna T S and Sulaiman S T N (2018) Formulation of Betel Leaf (Piper Betle L.) Essential Oil Patch Buccal with Variation CMC-Na and Carbopol as Mucoadhesive Polymers. *Pharmaceutics J*. **14**, 1, 22-23. DOI:10.22146/ farmaseutik.v14i1.41925

White S C and Pharoah M J (2014) *Oral Radiology Principles and Interpretations*. **7**th ed. St. Louis, Missouri: Elsevier Mosby. p. 16-17, 30-32, 153, 166.

Xotlanihua-Gervacio M D C, Guerrero-Flores M C, Herrera-Moreno J F, Medina-Díaz I M, Bernal-Hernández Y Y and Barrón-Vivanco B S (2018) Micronucleus frequency is correlated with antioxidant enzyme levels in workers occupationally exposed to pesticides. *Environ. Scie. Poll. Res*. **25**, 31, 31558-31568. doi: 10.1007/s11356-018-3130-8

Yu L, Zhao M, Yang B, Zhao Q and Jiang Y (2007) Phenolics from hull of garcinia mangostana fruit and their antioxidant activities. *J. Food Chem*. **104**(1), 176-181. https://doi.org/ 10.1016/ j.foodchem.2006.11.018

Yusuf D, Rahardjo T and Syaifudin M (2018) Evaluation of Radiation Dose Relationship to DNA Cell Damage Using Comet Test. *Jurnal Sains dan Teknologi Nuklir Indonesia* **19**(1), 13-20. http:/ /dx.doi.org/10.17146/jstni.2018.19.1.3658

Zhang Y, Guo J, Qi Y, Shao Q and Liang J (2014) The prevention of radiation-induced DNA damage and apoptosis in human intestinal epithelial cells by salvianic acid A. *J Radiat Res Appl Sci*. **7**, 3, 274-85. https://doi.org/10.1016/j.jrras.2014.05.003

The Effect Of Mangosteen Pericarp (Garcinia Mangostana L.) Extract Mucoadhesive Gingival Patch On The Mda Levels And The Number Of Micronuclei Due To Panoramic Radiography Radiation

ORIGINALITY REPORT

8%	5%	6%	1%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	repository.unair.ac.id Internet Source	2%
2	Ashok Galav, Monalisa Borah, Chetan Sugandhi, Raju Rathod, Nupur Satija, Mansi Chauhan. "Attitude and practice of dental professionals towards using of advance radiographic technique: a cross-sectional descriptive study", Journal of Research in Dentistry, 2017 Publication	1%
3	media.neliti.com Internet Source	1%
4	"Functional Foods and Nutraceuticals", Springer Science and Business Media LLC, 2020 Publication	1%
5	Maria del Carmen Xotlanihua-Gervacio, Mirna Citlali Guerrero-Flores, José Francisco Herrera-	<1%

Moreno, Irma Martha Medina-Díaz et al. "Micronucleus frequency is correlated with antioxidant enzyme levels in workers occupationally exposed to pesticides", Environmental Science and Pollution Research, 2018
Publication

6	bioinformatics.fafu.edu.cn Internet Source	<1%
7	Angela Babetski Holton, Francy L. Sinatra, Jenny Kreahling, Amy J. Conway, David A. Landis, Soner Altiok. "Microfluidic Biopsy Trapping Device for the Real-Time Monitoring of Tumor Microenvironment", PLOS ONE, 2017 Publication	<1%
8	www.science.gov Internet Source	<1%
9	Rurie Ratna Shantiningsih, Silviana Farrah Diba, Anggun Dwi Andini. "β-carotene gingival mucoadhesive patch to prevent panoramic radiography exposure's effect on GCF", AIP Publishing, 2019 Publication	<1%
10	www.medicolegalupdate.org Internet Source	<1%
11	www.jidmr.com Internet Source	<1%

12	Lisdiana, WH Nugrahaningsih, I Nufus. "Analysis of malondialdehyde and superoxide dismustase levels after exposure of electric cigarette in rats", Journal of Physics: Conference Series, 2020 Publication	<1%
13	Bright Fafali Dogbey, Salis Ibrahim, John Apirigi-Eta Abobe. "Comparison of Antioxidant and Antimicrobial Activities of Acetone and Water Extracts of Theobroma cacao Beans", Advances in Microbiology, 2020 Publication	<1%
14	orca.cf.ac.uk Internet Source	<1%
15	Zuzana Freitinger Skalická, Friedo Zölzer, Ladislav Beránek, Jaroslav Racek. "Indicators of oxidative stress after ionizing and/or non-ionizing radiation: Superoxid dismutase and malondialdehyde", Journal of Photochemistry and Photobiology B: Biology, 2012 Publication	<1%
16	www.laser-therapy.us Internet Source	<1%
17	Ji-Soo Kim, Hokyun Kim, Bora Yim, Jae-Sung Rhee, Eun-Ji Won, Young-Mi Lee. "Identification and molecular characterization of two Cu/Zn-	<1%

SODs and Mn-SOD in the marine ciliate Euplotes crassus : Modulation of enzyme activity and transcripts in response to copper and cadmium", Aquatic Toxicology, 2018
Publication

---

18 Suwoto, H. Adrial, W. Luthfi, T. Setiadipura, Zuhair. "Effect of boron impurity and graphite thermal neutron scattering on criticality calculation of Indonesian experimental power reactor", AIP Publishing, 2019 <1%
Publication

---

19 www.innspub.net <1%
Internet Source

---

20 M I Sari, N B Rahmat, D W Wijaya. "Effect of Prunus Dulcis Extract against Total Cholesterol Level in Mice that Given Monosodium Glutamate", IOP Conference Series: Materials Science and Engineering, 2018 <1%
Publication

Exclude quotes	Off	Exclude matches	< 7 words
Exclude bibliography	On		

The Effect Of Mangosteen Pericarp (Garcinia Mangostana L.) Extract Mucoadhesive Gingival Patch On The Mda Levels And The Number Of Micronuclei Due To Panoramic Radiography Radiation

GRADEMARK REPORT

FINAL GRADE

/0

GENERAL COMMENTS

Instructor

PAGE 1

PAGE 2

PAGE 3

PAGE 4

PAGE 5

PAGE 6