

ANTI-ANTI-INFLAMMATORY ACTIVITY OF HERBAL FORMULATION PREPARED USING MINT AND GREEN TEA

Formatted: English (New Zealand)

ABSTRACT:

Aim:-

The aim of ~~my this~~ study is to evaluate the anti-inflammatory activity of herbal formulation prepared using mint and green tea.

Introduction:

Green tea is a 'non-fermented' tea, and contains more catechins than black tea or oolong tea. ~~Green tea and e~~Epigallocatechin 3-gallate in green tea, suppress the gene and/or protein expression of inflammatory cytokines and inflammation-related enzymes. Mint ~~have has a the~~ potent anti-inflammatory activity in the croton oil-induced mouse ear edema model.

Materials and methods

Preparation of herbal formulation:

A mixture was prepared by adding 1 g of tea leaves and 1 g of powdered mint to 100 ml of distilled water. ~~To 100 ml of distilled water, 1 g of tea leaves and 1 g of powdered mint is added.~~

This mixture was heated for about 15-20 minutes and then filtered using filter paper. The mixture was again heated and concentrated ~~from 70 ml~~ to a final volume of 20 ml.

Result: At 20 µl there is 59 percent of inhibition, at 50 µl there is 90 % of inhibition, whereas in the standard there is only 40% of inhibition. Thus as the concentration increases the anti-inflammatory activity of the extract increases.

Conclusion:

From this study we can conclude that green tea and mint have a great anti-inflammatory property. Anti-inhibitory zone ranging from 90 and is indicating that it is higher than the standard diclofenac sodium which has only 40% of inhibition.

Keywords: Green tea, mint, anti-inflammatory, epigallocatechin

Formatted: English (New Zealand), Highlight

Formatted: English (New Zealand)

Comment [G1]: This only describe a part of the method followed in this study. Also, this part needs to be rewritten in a concise manner.

Comment [G2]: The powder is prepared or purchased? If prepared please explain the methods followed.

Formatted: English (New Zealand)

Comment [G3]: Type and number?

Comment [G4]: Arrange in alphabetical order.

INTRODUCTION:

Green tea is a 'non-fermented' tea, and has more catechins when compared to black tea or oolong tea. Catechins occur in vitro and in vivo as strong antioxidants. Its content of some minerals and vitamins ~~heightens the~~ heightens the antioxidant potential of ~~this type of tea~~ green tea (1). Tea, a product made up from leaf and bud of the plant *Camellia sinensis*, is the second most consumed beverage in the world, well ahead of coffee, beer, wine and carbonated soft drinks (2). Green tea is made with fresh tea leaves which are boiled to avoid fermentation, resulting in a dry and stable product. Catechin, represented by epicatechin, epicatechin 3-gallate, 3-epigallocatechin and epigallocatechin 3-gallate, are the most important flavonoids in tea (3). Mint or menthol has a place with the Lamiaceae family, which contains around 15 to 20 plant species, including peppermint and spearmint (4). ~~Mints are aromatic, almost exclusively perennial herbs.~~ They have wide-spreading underground and overground stolons (5). Herbal sources have their starting points in antiquated societies (6) (7) (8) (9) (10) (11) (12) (13) (14) (15) (16) (17) (18) (19) (20). It includes the restorative utilization of plants to treat infections. Since old occasions, spices have been utilized as characteristic medicines for different diseases, including viral contaminations. ~~Treatment with home-grown plants is viewed as protected as there are no or insignificant results~~ (21). The inflammatory process is a reaction to an injurious stimulus—~~eliciting~~ elicited by a ~~wide assortments of poisonous agents~~ wide assortment of poisonous agents for diseases, contaminations, antibodies or actual wounds. Inflammation is a substantial reaction to injury, contamination or annihilation, portrayed by heat, redness, agony, growing and upset physiological capacities (22). Inflammation is considered as a significant basis reaction responsible for symptoms of various chronic disorders such as cancer, septic shock, diabetes, atherosclerosis and obesity (23–25). The inflammatory response is a process involving complex interactions among inflammatory molecules that prompts tissue to respond to traumatic, infectious, posts ischemic ~~and~~ toxic, or autoimmune injury. Numerous plants have ~~exhibited good~~ exhibited good NO inhibition (26). Green tea extract ~~may could~~ be potentially

Comment [G5]: Repetition of abstract. Rewrite it.

Comment [G6]: Reference?

Comment [G7]: Occurs where?

Comment [G8]: Square brackets. Change throughout the manuscript.

Formatted: Font: Italic, English (New Zealand)

Formatted: English (New Zealand)

Comment [G9]: Combine these sentences.

Formatted: Font: 11 pt, English (New Zealand)

Comment [G10]: Delete unnecessary citations. For a general statement like this, maximum of two citations are sufficient.

Formatted: English (New Zealand)

Comment [G11]: Unclear sentence. Please rewrite.

Comment [G12]: Rephrase the sentence

Comment [G13]: What is this?

Comment [G14]: Can not use two model vers

used as oral rinse anti-inflammatory drug for treatment and prevention of oral inflammatory diseases (27,28). Mint ~~have~~ ~~has~~ a potent anti-inflammatory activity in the croton oil-induced mouse ear edema model, and the possible action mechanism might be attributed to its inhibitory effect on the production of NO and PGE2 (23,24). Tannins are phenolics constituents and potent for ~~the~~ treating ~~the~~ inflamed tissues (29,30). Green tea and epigallocatechin 3-gallate, subdues the gene protein expression of inflammatory cytokines and inflammation-related enzymes (31). Green tea ~~supplements are~~ ~~supplements are~~ accessible at pharmacies and hospitals. They can be found in liquid syrup or capsule form (32). ~~Plants give hundreds~~ and thousands of different chemical constituents with varying biological activities and have been utilised in the treatment of various human ailments. Herbal medicine has been practiced in rural areas since time immemorial (24). The health benefits of green tea depend on its bioavailability after consumption. In the body, the components in green tea may undergo metabolic processing such as glucuronidation, methylation, and sulfation, which produces active metabolites (33). Green tea has an antiproliferative activity on hepatoma cells and a hypolipidemic activity in hepatoma-treated rats, as well as the prevention of hepatotoxicity (34). EGCG of green tea extract is cytotoxic, and higher consumption of green tea can exert acute cytotoxicity in liver cells, a major metabolic organ in the body (35). Green tea and green tea polyphenols are reported to inhibit carcinogenesis and malignant behavior in several diseases (36). ~~Cancer~~ is one of the major diseases that cause a high number of deaths globally (37). ~~The prime~~ reason for the high mortality rate of patients suffering from oral cancer is the delay in the diagnosis of the type and grade of oral cancer and also in the offering of prompt treatment (38). Mint essential oil are extensively used as flavorings in breath fresheners, drinks, antiseptic mouth rinses, toothpaste, chewing gum and ~~candies~~ ~~candies~~, such as ~~mintas~~ ~~mint~~ candy and mint chocolate. Mint was originally used as a medicinal herb to treat stomach ache, chest pain and treating irritable bowel syndrome (39). The liver is vulnerable to many forms of chronic injury due to its unique anatomic location and functions. It has the remarkable ability to scavenge the free radicals generated during the metabolism of various drugs (40). Green tea consumption is associated with decreased fasting glucose levels and A1C levels, as well as reduced fasting insulin levels (41). ~~Diabetes~~ is a chronic metabolic disorder steadily increasing prevalence worldwide. It is characterized by hyperglycemia with altered carbohydrate, protein, and lipid metabolism. This may be attributed to insulin inactivity or resistance, as a direct result of destruction or dysfunction of the beta-cells

Comment [G15]: These studies confirm the anti-inflammatory activity of green tea. Then why the author used may or could in this sentence?

Comment [G16]: Please rearrange the paragraph. Discuss the green tea and mint separately. Please do not mix them up.

Comment [G17]: This introductory sentence should be at the start of the paragraph.

Formatted: English (New Zealand)

Comment [G18]: Extended form at first mention.

Comment [G19]: Why it is discussed in this manuscript? Is it relevant to this manuscript?

Comment [G20]: Why it is discussed in this manuscript? Is it relevant to this manuscript?

Comment [G21]: Why it is discussed in this manuscript? Is it relevant to this manuscript?

of the pancreas (42,43). Usage of nonsteroidal anti-inflammatory drugs has proven to give side effects such as stomach pain, heartburn, and stomach ulcers. Hence, it is time for us to go back to nature and promote herbal medicines rather than the allopathic medicines for having the least side effects(44,45). Our team has extensive knowledge and research experience that has translate into high quality publications(46-50),(51),(52),(53),(54),(55),(56),((48,57,58),(6,59-62),.(63),(64)

Comment [G22]: What is the research gap?

Formatted: Font: 11 pt, English (New Zealand)

Formatted: English (New Zealand)

Formatted: Font: 11 pt, English (New Zealand)

Comment [G23]: Remove all these references.

Comment [G24]: ?????

Formatted: English (New Zealand)

The aim of this study is to evaluate the anti-inflammatory activity of herbal formulations prepared using mint and green tea.

Materials and methods:

Preparation of herbal formulation:

To 100 ml of distilled water, 1 g of tea leaves and 1 g of powdered mint is added-. This mixture was heated for about 15-20 minutes and then filtered using filter paper. The mixture was again heated and concentrated from 70 ml to for a final volume of 20 ml.

Comment [G25]: Reference?

Comment [G26]: Water extract or infusion?

Formatted: English (New Zealand)

Comment [G27]: A repetition of abstract. Please rephrase it.

Anti-inflammatory activity:

The anti-inflammatory activity for -green tea and mint was tested by the following convention-.

A 0.05 ml of green tea and mint herbal infusion was added to 0.45 ml bovine serum albumin -albumin. Percentage of protein denaturation was determined utilising following equation

% inhibition = $\frac{\text{Absorbance of control} - \text{Absorbance of sample}}{\text{Absorbance of control}} \times 100$

Absorbance of control

Comment [G28]: Reference?

Comment [G29]: How many

Formatted: English (New Zealand)

Formatted: English (New Zealand)

Formatted: English (New Zealand)

Comment [G30]: What is the control?

Formatted: English (New Zealand)

Statistical analysis?

Formatted: Highlight

Formatted: English (New Zealand)

Results and discussion:-

At 20 µl there is 59 percent of inhibition, at 40 µl there is 80 % of inhibition and at 50 µl there is 90 % of inhibition, whereas in the standard there is only 40% of inhibition. Thus, as the concentration increases the anti-inflammatory activity of the extract increases.

Formatted: English (New Zealand)

Formatted: English (New Zealand)

Formatted: English (New Zealand)

Comment [G31]: Do mean separation and mentioned whether this is significant or not.

Formatted: English (New Zealand)



Figure 1: Synthesis-Extraction of herbal formulation-infusion of Green-tea and Mint.

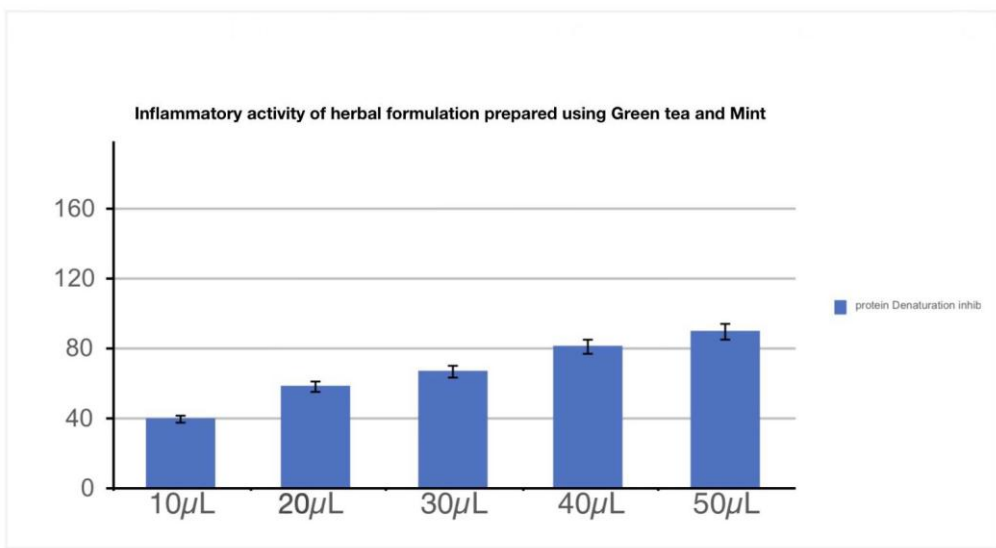
Formatted: English (New Zealand)

Formatted: English (New Zealand)

Formatted: English (New Zealand)

Formatted: English (New Zealand)

Formatted: English (New Zealand)



Comment [G32]: Remove the heading in the figure. The figure caption is only sufficient.

Remove the legend of the graph.

Formatted: English (New Zealand)

Comment [G33]: Add the Y and X axis and units.

Comment [G34]: A mean separation needs to be performed to identify the significant difference in anti-inflammatory activity between concentration of infusions.

Formatted: English (New Zealand)

Formatted: English (New Zealand)

Formatted: English (New Zealand)

Formatted: English (New Zealand)

Formatted: English (New Zealand)

Figure 2: The bar graph represents the anti- inflammatory activity of herbal formulation of Green-tea and Mint. X axis represents the concentration in the microliter and Y

~~axis represents the percentage of inhibition, data implies as~~ The data represented in mean \pm SEM (n=????).

Conclusion:

From this study we can conclude that green tea and mint have a **great** anti-inflammatory property. **Anti-inhibitory zone** ranging from 90 and is indicating that it is higher than the standard diclofenac sodium which has only 40% of inhibition.

Formatted: English (New Zealand)

Formatted: Font: 11 pt, English (New Zealand)

Formatted: English (New Zealand)

Formatted: English (New Zealand)

Comment [G35]: ????

Formatted: English (New Zealand)

Comment [G36]: Not discussed in results and discussion.

Formatted: English (New Zealand)

Formatted: English (New Zealand)

REFERENCES:

1. Cabrera C, Artacho R, Giménez R. Beneficial Effects of Green Tea—A Review [Internet]. Vol. 25, Journal of the American College of Nutrition. 2006. p. 79–99. Available from: <http://dx.doi.org/10.1080/07315724.2006.10719518>
2. Costa LM, Gouveia ST, Nóbrega JA. Comparison of heating extraction procedures for Al, Ca, Mg, and Mn in tea samples. Anal Sci. 2002 Mar;18(3):313–8.
3. Mota MA de L, de Lima Mota MA, Landim JSP, Targino TSS, da Silva SFR, da Silva SL, et al. Evaluation of the anti-inflammatory and analgesic effects of green tea (*Camellia sinensis*) in mice [Internet]. Vol. 30, Acta Cirurgica Brasileira. 2015. p. 242–6. Available from: <http://dx.doi.org/10.1590/s0102-865020150040000002>
4. Harley RM, Atkins S, Budantsev AL, Cantino PD, Conn BJ, Grayer R, et al. Labiatae [Internet]. Flowering Plants · Dicotyledons. 2004. p. 167–275. Available from: http://dx.doi.org/10.1007/978-3-642-18617-2_11
5. Aflatuni A, Uusitalo J, Ek S, Hohtola A. Variation in the Amount of Yield and in the

Extract Composition Between Conventionally Produced and Micropropagated Peppermint and Spearmint [Internet]. Vol. 17, Journal of Essential Oil Research. 2005. p. 66–70. Available from: <http://dx.doi.org/10.1080/10412905.2005.9698833>

6. Ezhilarasan D, Apoorva VS, Ashok VN. Syzygium cumini extract induced reactive oxygen species-mediated apoptosis in human oral squamous carcinoma cells. J Oral Pathol Med [Internet]. 2019 Feb [cited 2021 Sep 15];48(2). Available from: <https://pubmed.ncbi.nlm.nih.gov/30451321/>
7. Danda AK, Krishna TM, Narayanan V, Siddareddi A. Influence of primary and secondary closure of surgical wound after impacted mandibular third molar removal on postoperative pain and swelling--a comparative and split mouth study. J Oral Maxillofac Surg [Internet]. 2010 Feb [cited 2021 Sep 15];68(2). Available from: <https://pubmed.ncbi.nlm.nih.gov/20116700/>
8. Ramadurai N, Gurunathan D, Samuel AV, Subramanian E, Rodrigues SJL. Effectiveness of 2% Articaine as an anesthetic agent in children: randomized controlled trial. Clin Oral Investig [Internet]. 2019 Sep [cited 2021 Sep 15];23(9). Available from: <https://pubmed.ncbi.nlm.nih.gov/30552590/>
9. Sathivel A, Raghavendran HR, Srinivasan P, Devaki T. Anti-peroxidative and anti-hyperlipidemic nature of Ulva lactuca crude polysaccharide on D-galactosamine induced hepatitis in rats. Food Chem Toxicol [Internet]. 2008 Oct [cited 2021 Sep 15];46(10). Available from: <https://pubmed.ncbi.nlm.nih.gov/18706469/>
10. Panda S, Doraiswamy J, Malaiappan S, Varghese SS, Del Fabbro M. Additive effect of autologous platelet concentrates in treatment of intrabony defects: a systematic review and meta-analysis. J Investig Clin Dent [Internet]. 2016 Feb [cited 2021 Sep 15];7(1). Available from: <https://pubmed.ncbi.nlm.nih.gov/25048153/>
11. Neelakantan P, Varughese AA, Sharma S, Subbarao CV, Zehnder M, De-Deus G. Continuous chelation irrigation improves the adhesion of epoxy resin-based root canal sealer to root dentine. Int Endod J [Internet]. 2012 Dec [cited 2021 Sep 15];45(12). Available from: <https://pubmed.ncbi.nlm.nih.gov/22612994/>
12. Govindaraju L, Neelakantan P, Gutmann JL. Effect of root canal irrigating solutions on the compressive strength of tricalcium silicate cements. Clin Oral Investig [Internet]. 2017 Mar [cited 2021 Sep 15];21(2). Available from: <https://pubmed.ncbi.nlm.nih.gov/27469101/>
13. Sekhar CH, Narayanan V, Baig MF. Role of antimicrobials in third molar surgery: prospective, double blind, randomized, placebo-controlled clinical study. Br J Oral Maxillofac Surg [Internet]. 2001 Apr [cited 2021 Sep 15];39(2). Available from: <https://pubmed.ncbi.nlm.nih.gov/11286448/>
14. DeSouza SI, Rashmi MR, Vasanthi AP, Joseph SM, Rodrigues R. Mobile phones: the next step towards healthcare delivery in rural India? PLoS One [Internet]. 2014 Aug 18 [cited 2021 Sep 15];9(8). Available from: <https://pubmed.ncbi.nlm.nih.gov/25133610/>

15. Nasim I, Neelakantan P, Sujeer R, Subbarao CV. Color stability of microfilled, microhybrid and nanocomposite resins--an in vitro study. *J Dent* [Internet]. 2010 [cited 2021 Sep 15];38 Suppl 2. Available from: <https://pubmed.ncbi.nlm.nih.gov/20553993/>
16. Danda AK, Muthusekhar MR, Narayanan V, Baig MF, Siddareddi A. Open versus closed treatment of unilateral subcondylar and condylar neck fractures: a prospective, randomized clinical study. *J Oral Maxillofac Surg* [Internet]. 2010 Jun [cited 2021 Sep 15];68(6). Available from: <https://pubmed.ncbi.nlm.nih.gov/20303209/>
17. Molecular structure and vibrational spectra of 2,6-bis(benzylidene)cyclohexanone: A density functional theoretical study. *Spectrochim Acta A Mol Biomol Spectrosc*. 2011 Jan 1;78(1):113–21.
18. Putchala MC, Ramani P, Herald J, Sherlin, Premkumar P, Natesan A. Ascorbic acid and its pro-oxidant activity as a therapy for tumours of oral cavity – A systematic review [Internet]. Vol. 58, *Archives of Oral Biology*. 2013. p. 563–74. Available from: <http://dx.doi.org/10.1016/j.archoralbio.2013.01.016>
19. Neelakantan P, Grotra D, Sharma S. Retreatability of 2 mineral trioxide aggregate-based root canal sealers: a cone-beam computed tomography analysis. *J Endod*. 2013 Jul;39(7):893–6.
20. Suresh P, Marimuthu K, Ranganathan S, Rajmohan T. Optimization of machining parameters in turning of Al-SiC-Gr hybrid metal matrix composites using grey-fuzzy algorithm [Internet]. Vol. 24, *Transactions of Nonferrous Metals Society of China*. 2014. p. 2805–14. Available from: [http://dx.doi.org/10.1016/s1003-6326\(14\)63412-9](http://dx.doi.org/10.1016/s1003-6326(14)63412-9)
21. Herbal Sources Used by The Public Against Infections [Internet]. Vol. 12, *International Journal of Pharmaceutical Research*. 2020. Available from: <http://dx.doi.org/10.31838/ijpr/2020.sp1.015>
22. Bhattacharya S, Chandra S, Chatterjee P, Dey P. Evaluation of anti-inflammatory effects of green tea and black tea: A comparative in vitro study [Internet]. Vol. 3, *Journal of Advanced Pharmaceutical Technology & Research*. 2012. p. 136. Available from: <http://dx.doi.org/10.4103/2231-4040.97298>
23. Sun Z, Wang H, Wang J, Zhou L, Yang P. Chemical Composition and Anti-Inflammatory, Cytotoxic and Antioxidant Activities of Essential Oil from Leaves of *Mentha piperita* Grown in China. *PLoS One*. 2014 Dec 10;9(12):e114767.
24. Das A, Roy A, Rajeshkumar S, Lakshmi T. Anti-inflammatory Activity of Turmeric Oil Mediated Silver Nanoparticles [Internet]. Vol. 12, *Research Journal of Pharmacy and Technology*. 2019. p. 3507. Available from: <http://dx.doi.org/10.5958/0974-360x.2019.00596.1>
25. Karthikeyan G, Lakshmi T, Rajeshkumar S, Roy A, Gurunadhan D, Geetha RV, et al. Glucose Uptake Potential in L6 Myotubes by *Ficus racemosa* [Internet]. Vol. 10, *Indian Journal of Public Health Research & Development*. 2019. p. 3527. Available from:

<http://dx.doi.org/10.5958/0976-5506.2019.04132.9>

26. Anitha R, Prathoshni S, Lakshmi T. The effect of capsicum oleoresin on nitric oxide production and nitric oxide synthase gene expression in macrophage cell line [Internet]. Vol. 10, Pharmacognosy Research. 2018. p. 343. Available from: http://dx.doi.org/10.4103/pr.pr_46_18
27. Hagi A, Attin T, Schmidlin PR, Ramenzoni LL. Dose-dependent green tea effect on decrease of inflammation in human oral gingival epithelial keratinocytes: in vitro study [Internet]. Vol. 24, Clinical Oral Investigations. 2020. p. 2375–83. Available from: <http://dx.doi.org/10.1007/s00784-019-03096-4>
28. Cinthura C, Thangavelu L, Rajeshkumar S, Gurunadhan D, Pradeep Kumar R, Roy A. COX2 Inhibitory activity of Abutilon indicum-An Invitro Study [Internet]. Vol. 10, Indian Journal of Public Health Research & Development. 2019. p. 3523. Available from: <http://dx.doi.org/10.5958/0976-5506.2019.04131.7>
29. Harborne JB. Phytochemical Methods: A Guide to Modern Techniques of Plant Analysis. Springer Science & Business Media; 2012. 278 p.
30. Aafreen MM, Maajida Aafreen M, Anitha R, Preethi RC, Rajeshkumar S, Lakshmi T. Anti-Inflammatory Activity of Silver Nanoparticles Prepared from Ginger Oil—An Invitro Approach [Internet]. Vol. 10, Indian Journal of Public Health Research & Development. 2019. p. 145. Available from: <http://dx.doi.org/10.5958/0976-5506.2019.01552.3>
31. Ohishi T, Goto S, Monira P, Isemura M, Nakamura Y. Anti-inflammatory Action of Green Tea. *Antiinflamm Antiallergy Agents Med Chem*. 2016;15(2):74–90.
32. Lee F, Bae KH, Ng S, Yamashita A, Kurisawa M. Hyaluronic acid–green tea catechin conjugates as a potential therapeutic agent for rheumatoid arthritis [Internet]. Vol. 11, RSC Advances. 2021. p. 14285–94. Available from: <http://dx.doi.org/10.1039/d1ra01491a>
33. Reyaert W. An Update on the Health Benefits of Green Tea [Internet]. Vol. 3, Beverages. 2017. p. 6. Available from: <http://dx.doi.org/10.3390/beverages3010006>
34. Crespy V, Williamson G. A Review of the Health Effects of Green Tea Catechins in In Vivo Animal Models [Internet]. Vol. 134, The Journal of Nutrition. 2004. p. 3431S – 3440S. Available from: <http://dx.doi.org/10.1093/jn/134.12.3431s>
35. Schmidt M, Schmitz H-J, Baumgart A, Guédon D, Netsch MI, Kreuter M-H, et al. Toxicity of green tea extracts and their constituents in rat hepatocytes in primary culture. *Food Chem Toxicol*. 2005 Feb;43(2):307–14.
36. Miyata Y, Matsuo T, Araki K, Nakamura Y, Sagara Y, Ohba K, et al. Anticancer Effects of Green Tea and the Underlying Molecular Mechanisms in Bladder Cancer. *Medicines (Basel)* [Internet]. 2018 Aug 10;5(3). Available from: <http://dx.doi.org/10.3390/medicines5030087>

37. Sharma P, Mehta M, Dhanjal DS, Kaur S, Gupta G, Singh H, et al. Emerging trends in the novel drug delivery approaches for the treatment of lung cancer. *Chem Biol Interact.* 2019 Aug 25;309:108720.
38. Suhasini SJ, Jennifer Suhasini S, Roy A, Sosa G, Lakshmi T. The Cytotoxic effect of *Caralluma fimbriata* on KB cell lines [Internet]. Vol. 12, *Research Journal of Pharmacy and Technology.* 2019. p. 4995. Available from: <http://dx.doi.org/10.5958/0974-360x.2019.00865.5>
39. Jamila F, Mostafa E. Ethnobotanical survey of medicinal plants used by people in Oriental Morocco to manage various ailments. *J Ethnopharmacol.* 2014 May 28;154(1):76–87.
40. Ezhilarasan D. Oxidative stress is bane in chronic liver diseases: Clinical and experimental perspective [Internet]. Vol. 19, *Arab Journal of Gastroenterology.* 2018. p. 56–64. Available from: <http://dx.doi.org/10.1016/j.ajg.2018.03.002>
41. Sakuma T, Takase H, Hase T, Tokimitsu I. Green Tea Polyphenols in Weight Management (Obesity) and Diabetes [Internet]. *Green Tea Polyphenols.* 2013. p. 157–76. Available from: <http://dx.doi.org/10.1201/b14878-9>
42. Anitha R, Ashwini S. Antihyperglycemic activity of *Caralluma fimbriata*: An In vitro approach [Internet]. Vol. 13, *Pharmacognosy Magazine.* 2017. p. 499. Available from: http://dx.doi.org/10.4103/pm.pm_59_17
43. Anitha R, Aneesa N, Varghese S. Antidiabetic activity of ajwain oil in different in vitro models [Internet]. Vol. 11, *Journal of Pharmacy And Bioallied Sciences.* 2019. p. 142. Available from: http://dx.doi.org/10.4103/jpbs.jpbs_128_18
44. P S, Santhanam P, Rajeshkumar S, Lakshmi T, Roy A. Antifungal activity of neem and Aloe vera formulation mediated zirconium oxide nanoparticles [Internet]. Vol. 10, *International Journal of Research in Pharmaceutical Sciences.* 2019. p. 2864–8. Available from: <http://dx.doi.org/10.26452/ijrps.v10i4.1565>
45. Krishna RN, Anitha R, Ezhilarasan D. Aqueous extract of fruit pulp exhibits antihyperglycaemic activity. *Avicenna J Phytomed.* 2020 Sep;10(5):440–7.
46. Rajeshkumar S, Kumar SV, Ramaiah A, Agarwal H, Lakshmi T, Roopan SM. Biosynthesis of zinc oxide nanoparticles using *Mangifera indica* leaves and evaluation of their antioxidant and cytotoxic properties in lung cancer (A549) cells. *Enzyme Microb Technol.* 2018 Oct;117:91–5.
47. Nandhini NT, Rajeshkumar S, Mythili S. The possible mechanism of eco-friendly synthesized nanoparticles on hazardous dyes degradation. *Biocatal Agric Biotechnol.* 2019 May 1;19:101138.
48. Vairavel M, Devaraj E, Shanmugam R. An eco-friendly synthesis of *Enterococcus* sp.–mediated gold nanoparticle induces cytotoxicity in human colorectal cancer cells. *Environ Sci Pollut Res.* 2020 Mar 1;27(8):8166–75.

49. Gomathi M, Prakasam A, Rajkumar PV, Rajeshkumar S, Chandrasekaran R, Anbarasan PM. Green synthesis of silver nanoparticles using *Gymnema sylvestre* leaf extract and evaluation of its antibacterial activity [Internet]. Vol. 32, South African Journal of Chemical Engineering. 2020. p. 1–4. Available from: <http://dx.doi.org/10.1016/j.sajce.2019.11.005>
50. Rajasekaran S, Damodharan D, Gopal K, Rajesh Kumar B, De Pours MV. Collective influence of 1-decanol addition, injection pressure and EGR on diesel engine characteristics fueled with diesel/LDPE oil blends. *Fuel*. 2020 Oct 1;277:118166.
51. Santhoshkumar J, Sowmya B, Venkat Kumar S, Rajeshkumar S. Toxicology evaluation and antidermatophytic activity of silver nanoparticles synthesized using leaf extract of *Passiflora caerulea*. *S Afr J Chem Eng*. 2019 Jul;29:17–23.
52. Raj R K, D E, S R. β -Sitosterol-assisted silver nanoparticles activates Nrf2 and triggers mitochondrial apoptosis via oxidative stress in human hepatocellular cancer cell line. *J Biomed Mater Res A*. 2020 Sep;108(9):1899–908.
53. Saravanan M, Arokiyaraj S, Lakshmi T, Pugazhendhi A. Synthesis of silver nanoparticles from *Phenerochaete chrysosporium* (MTCC-787) and their antibacterial activity against human pathogenic bacteria. *Microb Pathog*. 2018 Apr;117:68–72.
54. Gheena S, Ezhilarasan D. Syringic acid triggers reactive oxygen species-mediated cytotoxicity in HepG2 cells. *Hum Exp Toxicol*. 2019 Jun 1;38(6):694–702.
55. Ezhilarasan D, Sokal E, Najimi M. Hepatic fibrosis: It is time to go with hepatic stellate cell-specific therapeutic targets. *Hepatobiliary Pancreat Dis Int*. 2018 Jun;17(3):192–7.
56. Ezhilarasan D. Oxidative stress is bane in chronic liver diseases: Clinical and experimental perspective. *Arab J Gastroenterol*. 2018 Jun;19(2):56–64.
57. Gomathi AC, Xavier Rajarathinam SR, Mohammed Sadiq A, Rajeshkumar S. Anticancer activity of silver nanoparticles synthesized using aqueous fruit shell extract of *Tamarindus indica* on MCF-7 human breast cancer cell line. *J Drug Deliv Sci Technol*. 2020 Feb 1;55:101376.
58. Dua K, Wadhwa R, Singhvi G, Rapalli V, Shukla SD, Shastri MD, et al. The potential of siRNA based drug delivery in respiratory disorders: Recent advances and progress. *Drug Dev Res*. 2019 Sep;80(6):714–30.
59. Ramesh A, Varghese S, Jayakumar ND, Malaiappan S. Comparative estimation of sulfiredoxin levels between chronic periodontitis and healthy patients - A case-control study. *J Periodontol*. 2018 Oct;89(10):1241–8.
60. Arumugam P, George R, Jayaseelan VP. Aberrations of m6A regulators are associated with tumorigenesis and metastasis in head and neck squamous cell carcinoma. *Arch Oral Biol*. 2021 Feb;122:105030.
61. Joseph B, Prasanth CS. Is photodynamic therapy a viable antiviral weapon against COVID-

19 in dentistry? Oral Surg Oral Med Oral Pathol Oral Radiol. 2021 Jul;132(1):118–9.

62. Duraisamy R, Krishnan CS, Ramasubramanian H, Sampathkumar J, Mariappan S, Navarasampatti Sivaprakasam A. Compatibility of Nonoriginal Abutments With Implants: Evaluation of Microgap at the Implant-Abutment Interface, With Original and Nonoriginal Abutments. *Implant Dent*. 2019 Jun;28(3):289–95.
63. Gnanavel V, Roopan SM, Rajeshkumar S. Aquaculture: An overview of chemical ecology of seaweeds (food species) in natural products. *Aquaculture*. 2019 May 30;507:1–6.
64. Markov A, Thangavelu L, Aravindhana S, Zekiy AO, Jarahian M, Chartrand MS, et al. Mesenchymal stem/stromal cells as a valuable source for the treatment of immune-mediated disorders. *Stem Cell Res Ther*. 2021 Mar 18;12(1):192.

UNDER PEER REVIEW