

CYTOTOXIC EFFECT OF CORIANDER OLEORESIN AGAINST LUNG CANCER CELL LINE A549

ABSTRACT

Aim: The main aim of present study was to assess the cytotoxic effect of coriander oleoresin against lung cancer cell line A549.

Introduction: *Coriandrum sativum* (Coriander), part of the Umbelliferae family, is a herbaceous vine of Mediterranean and Middle Eastern origin. Coriander contains mainly essential oil and has antioxidant, diuretic, anti-diabetic anticonvulsant, hypnotic sedative, anti-mutagenic, antimicrobial, anthelmintic activity. Uncontrolled growth of cells and apoptosis resistance characterise cancer cells.

Materials and methods: Coriander oleoresin (product number: 4010000243) was obtained from Synthite Industries private limited. In the present study, lung cancer cell line A549 was treated with coriander oleoresin at different concentrations and later evaluated by MTT assay.

Results: The cytotoxic effect of coriander oleoresin on lung cancer cell line was proved; the drug concentration increased, the percentage of cell viability decreased proving its cytotoxic effect. The coriander oleoresin has shown a dose dependent cytotoxic effect on lung cancer cell lines. As the drug concentration increased, the percentage of cell viability decreased proving its cytotoxic effect. The IC₅₀ value was 80 µg/ml.

Conclusion: In the present study, coriander oleoresin showed a good cytotoxic effect on lung cancer cell lines which may be helpful in treatment of lung cancer. However more research is needed to understand the underlying mechanisms of the cytotoxicity property of the plants.

Keywords: coriander oleoresin, lung cancer, therapeutic properties, cytotoxic activity, new approach

Running title: Cytotoxic effect of coriander oleoresin against lung cancer cell line A549.

INTRODUCTION

Coriandrum sativum (Coriander) part of the Umbelliferae family, is a herbaceous vine of Mediterranean and Middle Eastern origin. Coriander contains mainly essential oil and has antioxidant, diuretic, anti-diabetic anticonvulsant, hypnotic sedative, anti-mutagenic, antimicrobial, anthelmintic activity. The effect of the commercial value of coriander depends on its physical properties, chemical composition, and bioactivity. Linalool (78.45 percent), alpha-pinene (5.03 percent), camphor (3.90 percent), gamma-terpinene (3.80 percent), D-limonene(2.58 percent) and geranyl acetate (2.13 percent) are the key components of Coriander oleoresin (1). Coriander oleoresin is a natural food additive. It is obtained by solvent extraction of fruits of *coriandrum sativum*. It is a dark brown volatile liquid used in the pharmaceutical industry. Fresh coriander's distinctive smell is due to the presence of aldehyde in volatile oil.(2).

Coriander seed is used by people for treatment. Coriander is used for problems of digestion, such as stomach pain, lack of appetite, hernia, nausea, diarrhoea, bowel spasms, and intestinal gas. It is often used to treat diseases caused by bacteria and fungi, such as measles, haemorrhoids, toothaches, worms, and joint pain. Coriander is used by some breast-feeding women to improve milk supply. In manufacturing, coriander is used in medications (3). Uncontrolled growth of cells and apoptosis resistance characterise cancer cells via mutations in key signalling molecules, which regulate pathways that are directly involved in regulating cell proliferation and apoptosis, these two main features are initiated in cancer cells (4).

Cell lines have been helpful in elucidating essential signalling pathways in lung cancers, as well as in developing therapeutic applications based on these studies. Lung cancer cell lines have been spread widely among the research community, which have used them to great effect, and this trend is expected to continue (5). In an article written by Bu- Yeo Kim et al, they stated that the seeds of *D. sophia* had potent cytotoxic effect on lung cancer cells A549. Seeds of *D. sophia* treatment induced dose dependent response in lung cancer cells A549 that showed down regulation of genes linked with metabolic functions and up- regulation of a large group of genes

linked with cell- growth related signalling pathways. It was found that the reciprocal regulatory mechanism may inhibit growth in human lung cancer A549 when treated with seeds of *D. sophia*. But the underlying mechanism must be understood for further future studies (6). Understanding the ability of herbal extracts and formulations to modulate metabolising enzymes will aid the health care system in providing adequate medication for patients and avoiding much of the side effects that come with it. Our team has extensive knowledge and research experience that has translated into high quality publications (7–11)(7–12). The main aim of this study was to assess the cytotoxic effect of coriander oleoresin against lung cancer cell line A549.

MATERIALS AND METHODS

Study setting: Cell line Research was conducted in Blue Lab, Saveetha dental College. The study was ethically approved by the Scientific Review Board, Saveetha Dental College, Chennai. [Ethical approval number: IHEC/SDC/UG-1926/21/91].

Reagents and extracts :

DMEM medium, 0.25% Trypsin-EDTA solution, sodium bicarbonate solution, bovine serum albumin (BSA), low melting agarose, MTT from Sigma Chemicals Co., St. Louis, USA. fetal bovine serum (FBS) and antibiotic/antimycotic solution, DMSO were from Himedia, Sodium phosphate monobasic and dibasic, sodium chloride, sodium hydroxide, sodium carbonate, hydrochloric acid and methanol were purchased from Sisco Research Laboratories (SRL) India.

Cell culture

The A549 cells were cultured in DMEM supplemented with 10% of phosphate buffer and 1% physiological saline. Cell cultures were maintained at 37° C in a fully humidified atmosphere containing 5% CO₂

Cell treatment

Coriander oleoresin was dissolved in 0.1% DMSO (v/v). A549 cells were plated at 1.2 X 10⁴ cells/cm². Twenty-four hours later, cells were fed with fresh expansion culture medium supplemented with different final concentrations of extract (20, 40, 80, 100, 120 and 140 µg/ml) or the corresponding volumes of the vehicle. After 24 h of treatment, cells were collected after 0.05% trypsin application. Cell viability was evaluated using the MTT assay.

MTT Assay

In vitro cytotoxicity assay the effect of coriander oleoresin on cell viability was measured by MTT assay following the method by Mosmann. Briefly, the cells (1 × 10⁵ cells per ml) were seeded in a 96 well microtiter plate (100 µl per well) with replications. Treatment was conducted for 24 with different concentrations (20, 40, 80, 100, 120 and 140 µg/ml) of coriander oleoresin. After incubation, 20 µl of 5 mg/ml MTT stock solution was added to each well and incubated for

4 h at 37 °C. The obtained formazan crystals were solubilized with DMSO and the absorbance was measured at 570 nm using a microplate reader (SpectraMax M5, Molecular Devices, USA). Cell viability (%) has been shown as a ratio of absorbance (A570) in treated cells to absorbance in control cells (0.1 % DMSO) (A570). The IC50 was calculated as the concentration of sample needed to reduce 50 % of the absorbance in comparison to the DMSO-treated control. Percent cell viability was calculated following the equation:

$$\text{Cell viability (\%)} = \{ \text{OD of (sample)} / \text{OD of (control)} \} \times 100$$

Morphological Study:

Based on MTT assay we selected the IC50 value of Coriander oleoresin for further studies. The characterisation of morphological changes in lung cancer cells before and after treatment with Coriander oleoresin were observed under phase contrast microscope.

Statistical Analysis:

All data obtained were analyzed and computed statistically (SPSS/10 Software Package; SPSS Inc., Chicago, IL, USA) using one-way ANOVA. Post-hoc testing was performed for inter comparisons using the LSD. In all tests, the level of statistical significance was set at $p < 0.05$.

RESULTS

In the present study, the cytotoxic effect of coriander oleoresin against lung cancer cell line A549 was evaluated using MTT assay. MTT assay provided a quick, simple and cost effective way for testing the cytotoxic activity of coriander oleoresin. In this study, lung cancer cell lines were treated with different concentrations of the extract of coriander oleoresin for 24 hours. Coriander oleoresin extract caused a dose dependent increase in the cytotoxic activity of lung cancer cell lines. Morphological changes and apoptosis of lung cancer cells were observed using coriander oleoresin under inverted phase contrast microscope at 20x magnification (figure 1). As the concentration of the extract increased, the percentage of cell viability decreased which depicted significance in cytotoxic activity of coriander oleoresin against lung cancer cell line (figure 2). The mean standard deviation (n=3) was calculated by student t- test using MS- Excel.

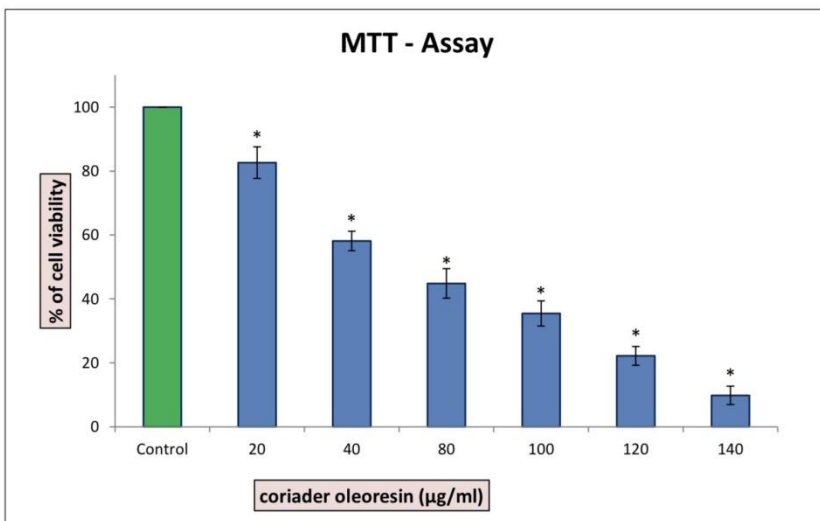


Figure 1: The graph represents the cytotoxic effects of coriander oleoresin on lung cancer cells. Cells were treated with coriander oleoresin (20, 40, 80, 100, 120 and 140 µM) for 24 hours, and cell viability was evaluated by MTT assay. Green denotes the control sample whereas blue denotes the different concentration of coriander oleoresin. X-axis denotes control of the different concentration of coriander oleoresin in. And the Y-axis denotes the percentage of cell viability. Data are shown as means \pm SD (n = 3). * compared with the control group, $p < 0.001$ by student-t test using MS- Excel. The IC50 value was found to be 30 µg/ml in 140 µg. The cell viability was also found to be 10%. Thereby the results shows that as the drug concentration increases, the percentage of cell viability decreases proving coriander oleoresin's cytotoxic effect.

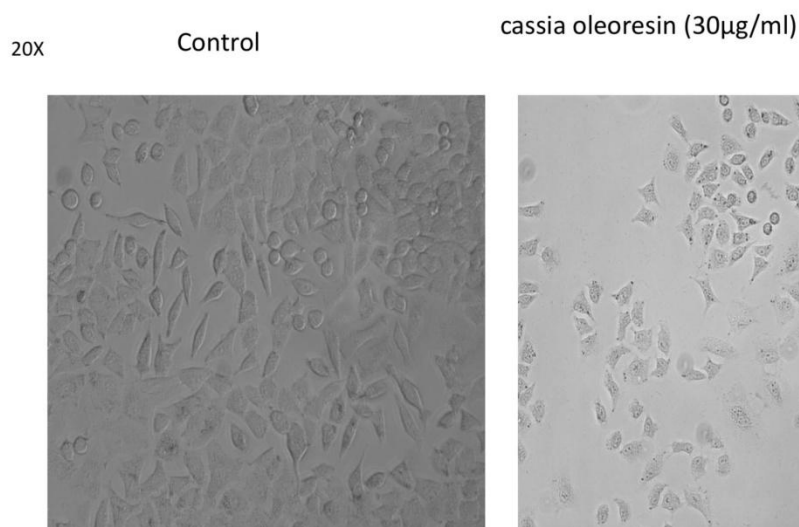


Figure 2: Assessment of cell morphology of lung cancer cells treated without or with coriander oleoresin. Cells were treated with coriander oleoresin (30 µg/ml) for 24 hours along with the control group. Images were obtained using an inverted Phase contrast microscope at 20x magnification.

DISCUSSION

In the present study, lung cancer cell line A549 was treated with coriander oleoresin at different concentrations and later evaluated by MTT assay (Figure 1, Figure 2). In another research done by Filomena Silva et al, coriander oil had antimicrobial activity against all bacteria that have been tested in the study. With the exception of *Bacillus cereus* and *Enterococcus faecalis*, coriander oil was found to have bactericidal activity against nearly all bacteria tested. Coriander oil's main mechanism of action was found as membrane disruption, which contributes to cell death. The findings of the study support the use of coriander oil in antibacterial formulations since it efficiently destroys pathogenic bacteria linked to foodborne diseases and hospital infections (13). P. Kowshihan et al has stated that after preparing coriander oleoresin mediated silver nanoparticles and confirmed by using UV- Visible spectroscopy, it was evaluated for its antifungal and antibacterial properties against *S. mutans*, *Lactobacillus*, *S. aureus* and *C. albicans*. It was seen that coriander oleoresin mediated silver nanoparticles had a good antimicrobial effect and can be used against the above mentioned infections (14).

The MTT assay, first defined by Tim Mosmann in 1983, is the most widely used viability assay in the world. The assay is based on metabolically active cell transferring of soluble yellow tetrazolium salt to insoluble purple formazan crystals. The tetrazolium salt can only be taken up

by living cells. Internalized tetrazolium salt was converted to purple formazan crystals by an enzyme (mitochondrial dehydrogenase) located in the mitochondria of living cells (15), (16).

Prathapan et al used the same method for studying the effect of lutein on differentiation and the cells were incubated at different concentrations later quantified using multiple plate readers at 490 nm. This preparation was similar to the preparation used in the present study (17),(18). The leaves of coriander show stronger antioxidant activity than seeds, but in both the parts of coriander, ethyl acetate extract showed the strongest ability. Addition of coriander to food increases antioxidant content and may have potential to act as a natural antioxidant to inhibit unwanted oxidation process(19) (20) (21) (22) (23) (24) (25) (26) (27) (28) (29) (30) (31) (32) (33). Surgery, radiofrequency, cryosurgery, chemotherapy, radiotherapy, targeted therapy with monoclonal antibodies, and angiogenesis inhibitors are all common therapeutic options. These are successful preventive screening programmes in treatment options. Due to a rise in cancer-related mortality and the harmful or toxic side effects of cancer chemotherapy and radiation therapy, new anticancer agents have been extracted from plants and also have been identified as screening of medicinal plants as a source of anticancer molecules (34),(35).

Coriander oleoresin exhibits antimicrobial activity against gram- negative and gram- positive bacteria, yeast, dermatophytes and filamentous fungi. Anti cancer effect of coriander oleoresin, source of dietary fibres and manganese, iron and magnesium helps increase levels of good cholesterol (HDL) (36). Selenium nanoparticles mediated by coriander oleoresin had strong anti-inflammatory efficacy, suggesting that it could be used for a healthy and environmentally sustainable synthesis of selenium nanoparticles for inflammatory conditions (37,38). Our team has extensive research expertise and has cooperated with several writers on a variety of issues over the last decade (39–46). The cytotoxic effect of coriander oleoresin on lung cancer cell line was proved; the drug concentration increased, the percentage of cell viability decreased proving its cytotoxic effect (45),(47)-(48) . Limitation seen in the present study is that the mechanism of cytotoxicity of coriander oleoresin could be understood better for future studies.The study may be extended in animal models in the future.

CONCLUSION

The use of coriander in daily life is quite common and it also has no side effects. The therapeutic value of coriander such as cytotoxic, antioxidant, antimicrobial activity plays a very important role in improving human health (49)-(50). From the present study, coriander oleoresin shows a dose-dependent cytotoxic effect on lung cancer cell line which may be helpful in treatment of lung cancer. However more research is needed to understand the underlying mechanisms of the cytotoxicity property of the plants.

REFERENCES

1. Rondon FCM, Bevilaqua CML, Accioly MP, de Moraes SM, de Andrade-Júnior HF, de Carvalho CA, et al. In vitro efficacy of *Coriandrum sativum*, *Lippia sidoides* and *Copaifera reticulata* against *Leishmania chagasi*. *Rev Bras Parasitol Vet.* 2012 Jul;21(3):185–91.
2. Salzer UJ. The analysis of essential oils and extracts (oleoresins) from seasonings--a critical review. *CRC Crit Rev Food Sci Nutr.* 1977;9(4):345–73.
3. Wangensteen H, Samuelsen AB, Malterud KE. Antioxidant activity in extracts from coriander [Internet]. Vol. 88, *Food Chemistry.* 2004. p. 293–7. Available from: <http://dx.doi.org/10.1016/j.foodchem.2004.01.047>
4. Yousef M, Vlachogiannis IA, Tsiani E. Effects of Resveratrol against Lung Cancer: In Vitro and In Vivo Studies. *Nutrients* [Internet]. 2017 Nov 10;9(11). Available from: <http://dx.doi.org/10.3390/nu9111231>
5. Gazdar AF, Girard L, Lockwood WW, Lam WL, Minna JD. Lung cancer cell lines as tools for biomedical discovery and research. *J Natl Cancer Inst.* 2010 Sep 8;102(17):1310–21.
6. Kim B-Y, Lee J, Park SJ, Bang O-S, Kim NS. Gene Expression Profile of the A549 Human Non-Small Cell Lung Carcinoma Cell Line following Treatment with the Seeds of *Descurainia sophia*, a Potential Anticancer Drug [Internet]. Vol. 2013, *Evidence-Based Complementary and Alternative Medicine.* 2013. p. 1–13. Available from: <http://dx.doi.org/10.1155/2013/584604>
7. 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.
8. 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.
9. 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.
10. Gomathi M, Prakasam A, Rajkumar PV, Rajeshkumar S, Chandrasekaran R, Anbarasan PM. Green synthesis of silver nanoparticles using *Gymnema sylvestris* 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>

11. Rajasekaran S, Damodharan D, Gopal K, Rajesh Kumar B, De Poures 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.
12. Website [Internet]. Available from: Veerasamy, R.; Roy, A.; Karunakaran, R.; Rajak, H. Structure–Activity Relationship Analysis of Benzimidazoles as Emerging Anti-Inflammatory Agents: An Overview. *Pharmaceuticals* 2021, 14, 663. <https://doi.org/10.3390/ph14070663>
13. Silva F, Ferreira S, Queiroz JA, Domingues FC. Coriander (*Coriandrum sativum* L.) essential oil: its antibacterial activity and mode of action evaluated by flow cytometry. *J Med Microbiol*. 2011 Oct;60(Pt 10):1479–86.
14. Majeed S, Samad M. Plant Mediated Synthesis of Silver Nanoparticles and its Antibacterial Effect [Internet]. Vol. 13, *Journal of Pure and Applied Microbiology*. 2019. p. 1267–72. Available from: <http://dx.doi.org/10.22207/jpam.13.2.69>
15. Koka P, Mundre RS, Rangarajan R, Chandramohan Y, Subramanian RK, Dhanasekaran A. Uncoupling Warburg effect and stemness in CD133 cancer stem cells from Saos-2 (osteosarcoma) cell line under hypoxia. *Mol Biol Rep*. 2018 Dec;45(6):1653–62.
16. Mandal S, Mandal M. Coriander (*Coriandrum sativum* L.) essential oil: Chemistry and biological activity [Internet]. Vol. 5, *Asian Pacific Journal of Tropical Biomedicine*. 2015. p. 421–8. Available from: <http://dx.doi.org/10.1016/j.apjtb.2015.04.001>
17. Prathapan A, Krishna MS, Lekshmi PC, Raghu KG, Nirmala Menon A. Modulation of adipogenesis and glucose uptake by *Curcuma longa* extract in 3T3L1 and L6 cell lines – An in vitro study [Internet]. Vol. 2, *Asian Pacific Journal of Tropical Disease*. 2012. p. S163–5. Available from: [http://dx.doi.org/10.1016/s2222-1808\(12\)60144-3](http://dx.doi.org/10.1016/s2222-1808(12)60144-3)
18. Meenapriya M, Anitha R, Lakshmi T. Effect of Lutein on Cytochrome P450 (Isoform CYP3A4) - An in vitro Study [Internet]. Vol. 10, *Pharmacognosy Journal*. 2018. p. 1093–5. Available from: <http://dx.doi.org/10.5530/pj.2018.6.185>
19. 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/>
20. 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/>
21. 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/>
22. 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/>
 23. 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/>
 24. 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/>
 25. 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/>
 26. 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/>
 27. 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/>
 28. 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/>
 29. 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/>
 30. 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.
 31. 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>

32. 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.
33. 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)
34. Ashwini S, Ezhilarasan D, Anitha R. Cytotoxic Effect of *Caralluma fimbriata* Against Human Colon Cancer Cells [Internet]. Vol. 9, *Pharmacognosy Journal.* 2017. p. 204–7. Available from: <http://dx.doi.org/10.5530/pj.2017.2.34>
35. Jain A, Anitha R, Rajeshkumar S. Anti inflammatory activity of Silver nanoparticles synthesised using Cumin oil [Internet]. Vol. 12, *Research Journal of Pharmacy and Technology.* 2019. p. 2790. Available from: <http://dx.doi.org/10.5958/0974-360x.2019.00469.4>
36. Vignesh S, Anitha R, Rajesh Kumar S, Lakshmi T. Evaluation of the Antimicrobial activity of Cumin oil mediated silver nanoparticles on Oral microbes [Internet]. Vol. 12, *Research Journal of Pharmacy and Technology.* 2019. p. 3709. Available from: <http://dx.doi.org/10.5958/0974-360x.2019.00634.6>
37. Narendra S, Roy A, Shanmugam R, Thangavelu L. Anti-inflammatory activity of nutmeg oleoresin mediated silver nanoparticles- An In- vitro study [Internet]. Vol. 39, *Biomedicine.* 2020. p. 234–8. Available from: <http://dx.doi.org/10.51248/.v39i2.186>
38. Swathy S, Roy A, Rajeshkumar S. Anti-inflammatory activity of Ginger oleoresin mediated Silver nanoparticles [Internet]. Vol. 13, *Research Journal of Pharmacy and Technology.* 2020. p. 4591. Available from: <http://dx.doi.org/10.5958/0974-360x.2020.00808.2>
39. Anandakumar P, Kamaraj S, Jagan S, Ramakrishnan G, Asokkumar S, Naveenkumar C, et al. Capsaicin inhibits benzo(a)pyrene-induced lung carcinogenesis in an in vivo mouse model [Internet]. Vol. 61, *Inflammation Research.* 2012. p. 1169–75. Available from: <http://dx.doi.org/10.1007/s00011-012-0511-1>
40. Cytotoxic Effect and Antibacterial Activity of Coriander Oleoresin Mediated Zinc Oxide Nanoparticles [Internet]. Vol. 12, *International Journal of Pharmaceutical Research.* 2020. Available from: <http://dx.doi.org/10.31838/ijpr/2020.sp1.411>
41. Raghunandhakumar S, Paramasivam A, Senthilraja S, Naveenkumar C, Asokkumar S, Binuclara J, et al. Thymoquinone inhibits cell proliferation through regulation of G1/S phase cell cycle transition in N-nitrosodiethylamine-induced experimental rat hepatocellular carcinoma. *Toxicol Lett.* 2013 Oct 23;223(1):60–72.
42. Microwave Assisted Synthesis and Characterization of Silver Nanoparticles Using

Ocimumbasilicum and its Anti-Inflammatory Activity against Human Blood Cells [Internet]. Vol. 5, International Journal of Science and Research (IJSR). 2016. p. 1422–8. Available from: <http://dx.doi.org/10.21275/v5i1.nov153036>

43. Asokkumar S, Naveenkumar C, Raghunandhakumar S, Kamaraj S, Anandakumar P, Jagan S, et al. Antiproliferative and antioxidant potential of beta-ionone against benzo(a)pyrene-induced lung carcinogenesis in Swiss albino mice. *Mol Cell Biochem*. 2012 Apr;363(1-2):335–45.
44. Paramasivam A, Raghunandhakumar S, Priyadharsini JV, Jayaraman G. In Vitro Anti-Neuroblastoma Activity of Thymoquinone Against Neuro-2a Cells via Cell-cycle Arrest. *Asian Pac J Cancer Prev*. 2015;16(18):8313–9.
45. 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
46. A MTAK, Mohamed Thamemul Ansari K, Roy A, Rajeshkumar S. Anti-inflammatory activity of cinnamon oil mediated silver nanoparticles -An in vitro study [Internet]. Vol. 10, *International Journal of Research in Pharmaceutical Sciences*. 2019. p. 2970–2. Available from: <http://dx.doi.org/10.26452/ijrps.v10i4.1579>
47. Dhayanithi J, Rajeshkumar S, Roy A, Lakshmi T. Preparation and Evaluation of Antifungal Activity of Arrow Root Mediated Selenium Nanoparticles Against Candida Albicans -. *Journal of Complementary Medicine Research*. 2020;11(5):83–8.
48. Role of Nanomedicine in Novel Corona Virus Pandemic: A perspective [Internet]. 2020 [cited 2021 Aug 31]. Available from: <http://bbrc.in/bbrc/role-of-nanomedicine-in-novel-corona-virus-pandemic-a-perspective/>
49. Rajendran R, Kunjusankaran RN, Sandhya R, Anilkumar A, Santhosh R, Patil SR. Comparative Evaluation of Remineralizing Potential of a Paste Containing Bioactive Glass and a Topical Cream Containing Casein Phosphopeptide-Amorphous Calcium Phosphate: An in Vitro Study. *Pesqui Bras Odontopediatria Clin Integr*. 2019 Mar 12;19(0):4668.
50. Kumar MS, Vamsi G, Sripriya R, Sehgal PK. Expression of matrix metalloproteinases (MMP-8 and -9) in chronic periodontitis patients with and without diabetes mellitus. *J Periodontol*. 2006 Nov;77(11):1803–8.