



Research Article

A COMPARATIVE STUDY ON INHALATION TOXICOLOGY BETWEEN AIR FRESHENERS OF SYNTHETIC AND NATURAL ORIGIN

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Article Received on: 01/09/20 Approved for publication: 29/09/20

DOI: 10.7897/2230-8407.110977

ABSTRACT

The main objective of this research is to design and formulate natural air freshener gel and evaluate the inhalational toxicity by comparing it with synthetic air freshener gel. The natural air freshener was prepared using natural gelatin and sandalwood oil as essential oil and the synthetic air freshener was prepared by using carbopol-940, Propylene glycol (10 % w/w), Ethanol (3% of total volume), triethanolamine as chemical composition and sandalwood as essential oil. The animals were acquired as per the CPCSEA guidelines, divided into groups and undergone with chronic exposure of prepared gels for 2 months. The animals were sacrificed, and the tissues were sent for histopathological studies. As per the results obtained from histopathology, it is observed that the animal groups which were allowed for the chronic inhalation of natural air freshener are safer when compared with the synthetic air freshener. The alveolar walls of the lungs became thicker and destroyed at some places for the animal group that was treated with synthetic air freshener and very less thick in case of natural ones. In case of liver, the normal polygonal shape of hepatocytes was distorted, their nuclei were enlarged, tissue was also damaged due to the appearance of blood streaks among the hepatocytes in synthetic treated group and the similar effects in natural are very less. In case of cerebral cortex of brain of mice, vacuolation was found in some areas due to damage and degeneration of neuronal cell body in synthetic treated group and these are very less in natural treated groups.

Keywords: Air freshener, triethanolamine, sandalwood oil, carbopol – 940, propylene glycol.

INTRODUCTION

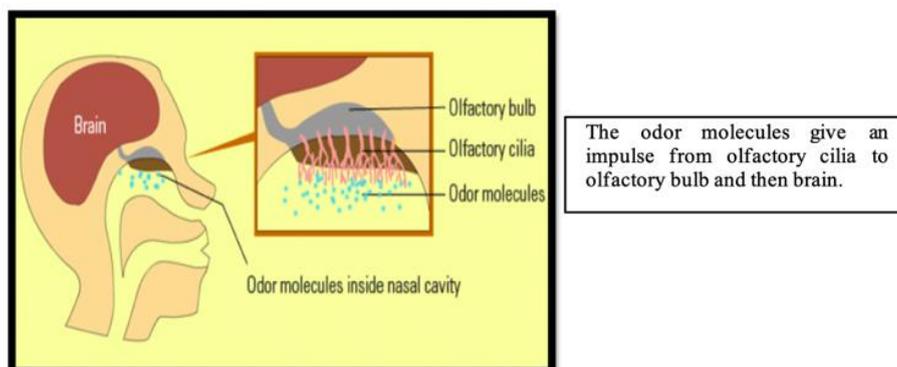
Many things in this world change according to the trend. Now due to the impact of globalization, everyone has the opportunity to access what the other person is able to, since every industry is reaching global standards. So, if there is any bright thing about the product and people start to use it, it is acceptable. Suppose if there is a dark shade of the product which is found very later, after the widespread of it, then it is difficult to eradicate it. In this current scenario, where perfumery merged with various other industries like disinfectants, clothing and air fresheners especially, to

enhance the fragrance and solubilize various fragrant ingredients, lot of harmful chemicals are being used, since they are available at cheaper range. Though they might not show immediate adverse reactions, they even can cause cancer on long term exposure.

Here, we chose to observe if there are any clear differences between natural ingredients-based air freshener and synthetic air freshener in terms of safety and efficiency.

To begin with the mechanism of the reception activity of olfactory bulb, it is shown with a diagrammatic representation:

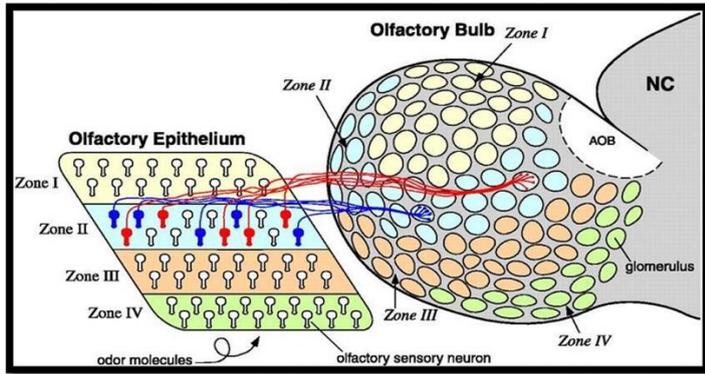
External View



<https://eschooltoday.com/science/the-five-senses/the-sense-of-taste.html>

Figure 1: Physiology of Olfaction (External)

Internal View



Since the signal or the molecules directly reaches the brain the response is very quick.

<https://science.sciencemag.org/content/286/5440/711>

Figure 2: Physiology of Olfaction (Internal)

There are many ailments that occur due to the toxicity of synthetic ingredients in air fresheners. These occur in less number during regular usage but are at times very severe. People who are working in the manufacturing units that produce these synthetic ingredients are more likely to show these side effects.

The common adverse effects shown are ¹⁻⁴

- **Autism:** a developmental disorder that disables the ability to communicate and interact.
- **ADHD (attention deficit hyperactivity disorder):** a condition where the patient has cognition failure.
- **Migraines:** the neurological condition in which the patient

has intense, debilitating headache.

- **Cancer:** formation of tumors due uncontrolled cell division. Here usually benign tumors are observed due to the inhalation toxicology of air fresheners.
- **Asthma:** the condition in which there is an obstruction of pathway in lungs due to the deposition of mucus.
- **Allergies and rashes:** usually these occur big and all of a sudden.
- **Reproductive toxicity:** this includes mainly degeneration of the gonads.

Side effects caused by various synthetic ingredients like benzene, toluene, formaldehyde and phthalates include⁵⁻⁶

Benzene

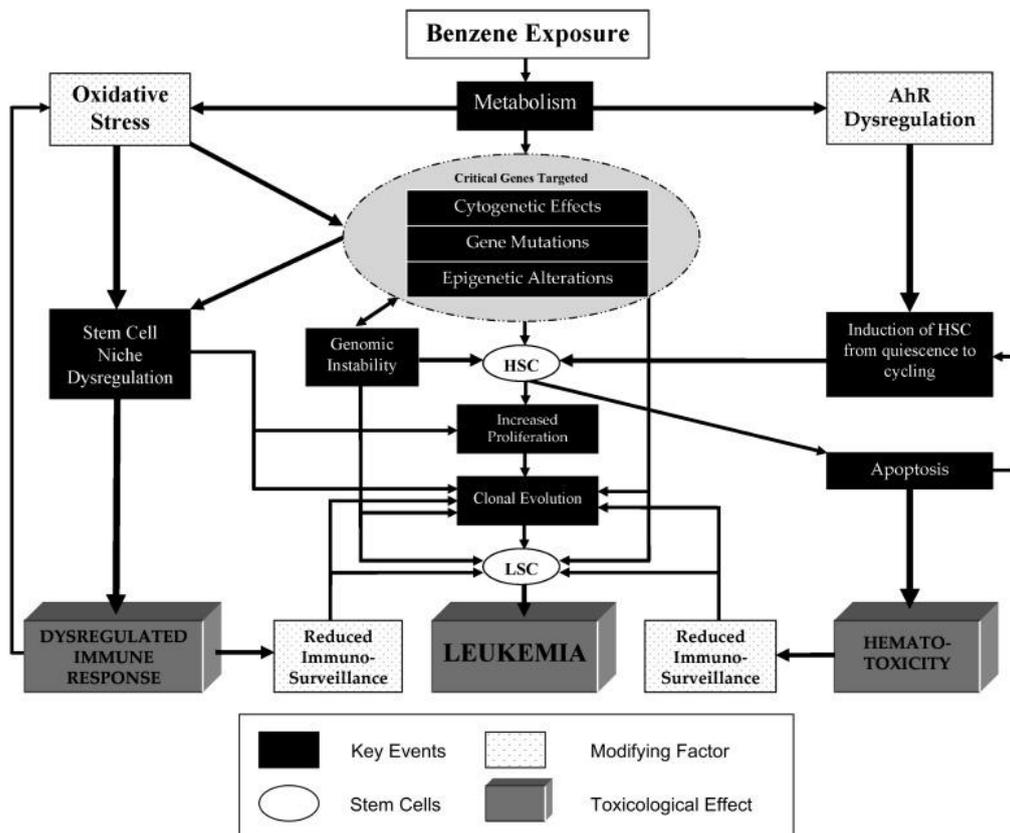


Figure 3: Effects of Benzene Exposure

Toluene

Table 1: Effects of toluene exposure

Acute effects	Chronic effects
<ul style="list-style-type: none"> • Irritation of eyes and respiratory pathways • Emotional liability: sudden mood changes • Dizziness • Slurred speech, Blurred vision • Lack of motor coordination • Illusions, hallucinations 	<ul style="list-style-type: none"> • Cognitive impairment (memory loss, difficulty in concentrating, attention deficit) • White matter abnormalities, particularly around brain ventricles • Ventricular enlargement • Loss of muscle strength • Cerebellar ataxia which leads to impaired motor coordination • Hearing loss, sight impairment, nystagmus

Advantages of Natural Air Freshener ⁷⁻¹¹

Flexible: Air freshener can be installed virtually anywhere in your building. It is designed not just for restrooms but also for use in areas such as offices, meeting rooms, care homes, hotels, reception areas, school classrooms or anywhere that a pleasant fragrance is desired.

Natural: Most air fresheners use natural essential oils to make their scents. The freshener contains no volatile organic compounds (VOC's) or aerosol products. And although most fragrances are strong and overpowering, Air fresheners leave a light, fresh fragrance behind.

Neutralizes: Some air fresheners simply will mask the smell of malicious odors instead of neutralizing the bad smell. However, air fresheners that eliminate odors completely as to avoid mixing uncomplimentary smells together are available in most departmental stores. It truly creates a fresh, clean smell completely void of ghastrly whiffs and scrunching noses.

Convenient: By choosing a good air freshener, you can easily refill the content as and when required.

Positive change in mood: There are situations when you are in a tremendous off mood. Even you feel like breaking your head. But, if suddenly if you get a fresh smell of lemon or natural flower, it

will instantly change your mood and you can easily get in to moon on with salinity and peace in mind.

Killing airborne pathogens: Some microorganisms and airborne pathogens are present in the environment that sometimes creates unhealthy atmosphere. If you can use the air fresheners with natural essential oil extracts, the airborne pathogens which are harmful for your body will be eradicated with the natural air fresheners. Even in your vehicles and bathrooms you can use these air fresheners in order to stay fresh and healthy.

MATERIALS AND METHODS

Experimental Animals

Mice of both sex (25-30g) were maintained for 7 days in the animal house of Chalapathi Institute of Pharmaceutical Sciences, Guntur under standard conditions temperature (24 ± 10 C), relative humidity (45-55%) and 12:12 light: dark cycle. The animals were fed with standard mice pellet and water ad libitum. The animals were allowed to acclimatize to laboratory conditions 48 h before the start of the experiment. 5 mice/group were used in all sets of experiments. All the experiments were conducted after obtaining permission from the Institutional Animal Ethics Committee (IAEC) Chalapathi Institute of Pharmaceutical Sciences, Guntur.

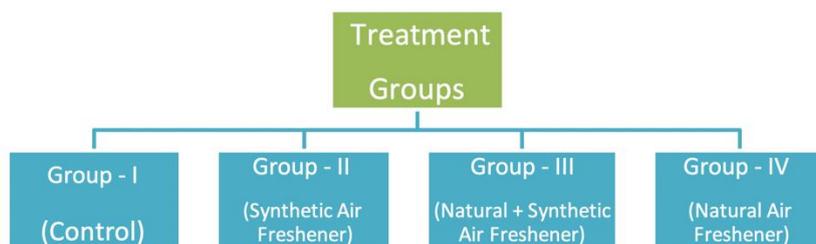


Figure 4: Treatment Groups

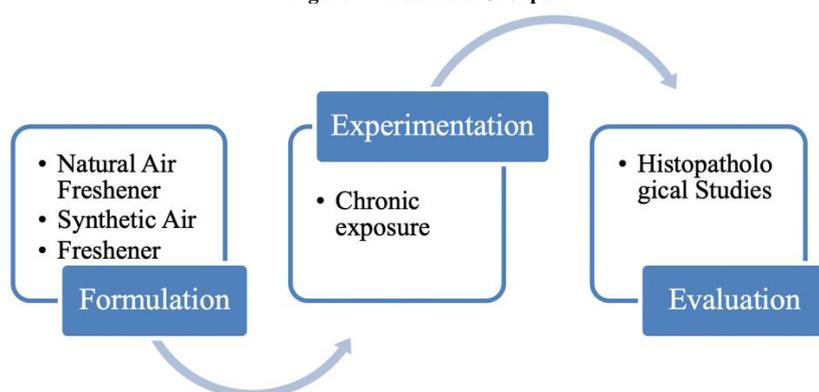


Figure 5: Experimental Design

Preparation of Synthetic Gel¹²⁻¹⁶

Synthetic gel was prepared using different concentrations of Carbopol 940 (0.75 and 1%), Na CMC (2 and 3%) and HPMC (8 and 10%) as gelling agents. The required amount of the polymer was dispersed in purified water in a beaker and stirred using a magnetic stirrer. Propylene glycol (10 % w/w) was added and

stirred until a homogenous gel was achieved. For gels containing Na CMC, the polymer was dispersed in the purified water and kept in a refrigerator overnight. The essential oil along with ethanol (3% of total volume) was added to the previous polymer dispersion with stirring. For Carbopol 940, adequate amount of triethanolamine was added to neutralize free carboxylic acid groups of carbopol 940 to pH 6.8 ± 0.2 .

Table 2: Formulation of Synthetic gel

Carbopol – 940 (%)	Propylene Glycol (%)	Essential Oil (%)	Ethanol (%)
0.75	10	3	3
1	10	3	3

Evaluation parameters¹⁷⁻²⁰

pH: pH of individual and polyherbal gel formulation was determined by using a pH meter.

Appearance and Homogeneity: The developed individual and polyherbal gels were evaluated for physical appearance and homogeneity by visual observation.

Viscosity: The viscosity of individual and polyherbal gels was measured by Brookfield viscometer (Model RVTDV II) at 100 rpm using spindle no. 6

Spreadability: The spreadability of the gel formulations was determined by measuring the spreading diameter of 1 g of gel between two horizontal plates (20 cm x 20 cm) after one min. The standard weight applied on the upper plate was 125gm.

Extrudability: The gel formulations were filled in standard capped collapsible aluminum tubes and sealed by crimping to the end. The weights of the tubes were recorded. The tubes were placed between two glass slides and were clamped. 0.5 gm was placed over the slides and then the cap was removed. The amount of the extruded gel was collected and weighed.

The percent of the extruded gel was calculated:

- >90% extrudability: Excellent
- >80% extrudability: good
- >70% extrudability: fair

Preparation of Natural Gel²¹⁻²⁷

In a small container, heat 3/4 cups of water and the salt. When the salt is completely dissolved, slowly add the gelatin, and stir until that is completely dissolved as well. If the gelatin was added too quickly, it might get a little sticky and “clumpy,” but just keep stirring until it dissolves.

Remove the container from the heat and then add the remaining liquid. Stir until fully blended and pour the mixture into the small containers.

Sandalwood as added and allow the whole content to dry.



Figure 6: Natural Gel made by Gelatin

Preclinical Studies²⁸⁻³⁴

Mice were divided into cages based on the treatment groups and the gels of various types prepared were set inside the cages. Every day the mice were exposed to the cages for 4 hours and the experimentation lasts for 2 months.

Meanwhile the changes in the animals’ weight and other skin diseases (if any) were observed to isolate them immediately if the problem persists.

Histopathological Studies

Animals were sacrificed by cervical dislocation and the tissues of lungs, liver and Brain were isolated for evaluating histopathological changes due to the chronic inhalation of animals of all groups. IAEC Number: 10/IAEC/CLPT/2019-20.

RESULTS AND DISCUSSION

Table 3: Evaluation parameters of Gel

Properties	Inference
pH	6.15
Appearance	Cherry red
Homogeneity	Good
Spreading Diameter (After 1 Min)	48mm
Viscosity (cp)	4700

Histopathological Studies

LIVER

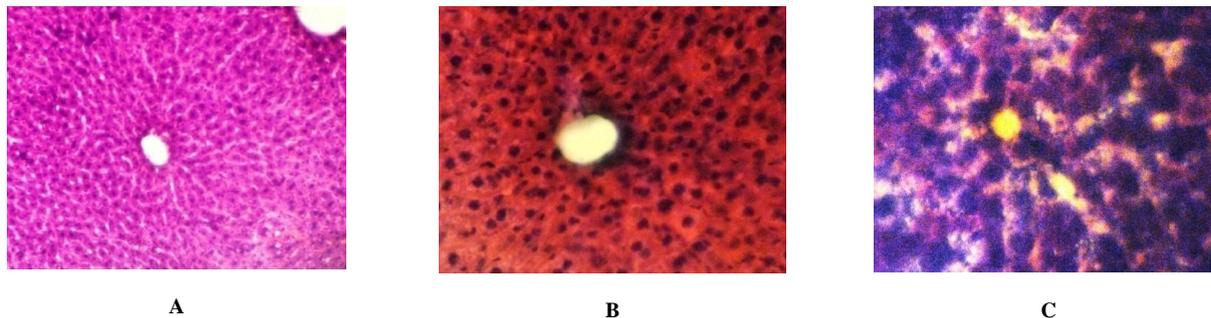


Figure 7: Histological Results of A) Normal B) Natural C) Synthetic treated liver

LUNGS

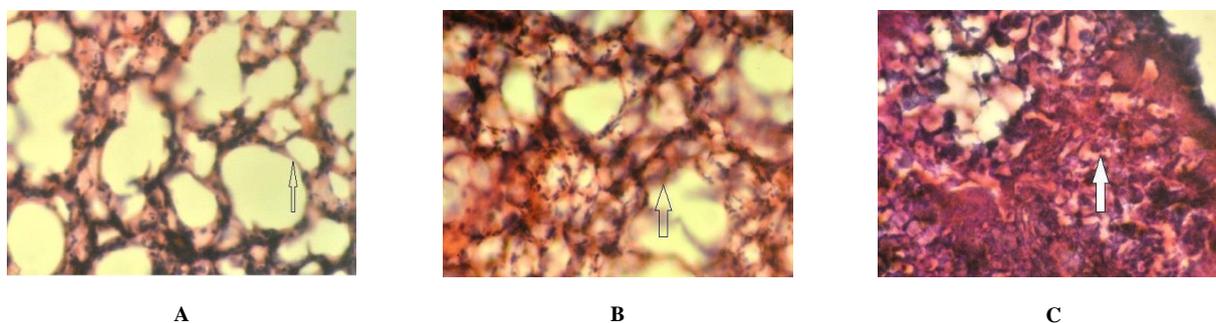


Figure 8: Histological Results of A) Normal B) Natural C) Synthetic treated lung

BRAIN

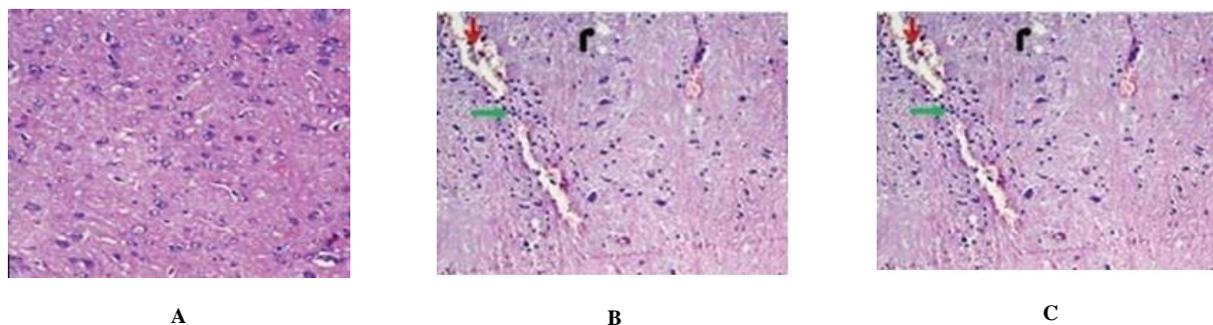


Figure 9: Histological Results of A) Normal B) Natural C) Synthetic treated Brain

DISCUSSION

As per the results obtained from histopathology, it is observed that the animal groups which were allowed for the chronic inhalation of natural air freshener are safer when compared with the synthetic air freshener. The alveolar walls of the lungs became thicker and destroyed at some places for the animal group that was treated with synthetic air freshener and very less thick in case of natural ones. In case of liver, the normal polygonal shape of hepatocytes was distorted, their nuclei were enlarged, tissue was also damaged due to the appearance of blood streaks among the hepatocytes in synthetic treated group and the similar effects in natural are very less. In case of cerebral cortex of brain of mice, vacuolation was found in some areas due to damage and degeneration of neuronal cell body in synthetic treated group and these are very less in natural treated groups.

CONCLUSION

The practice of chronic inhalation is not good always in case of both natural and synthetic air fresheners. The use of air fresheners must be minimized as per the convenience and should be dispensed with specific instructions. Anyhow, based on the current research, it was concluded that the air fresheners made of natural ingredients were safe when compared with synthetic air fresheners.

REFERENCES

1. Anne Steinemann; Health and societal effects from exposure to fragranced consumer products; *Preventive Medicine Reports.* 2017 Mar; 5: 45–47.
2. Anne Steinemann; *Fragranced consumer products: Exposures and effects from emissions: Air quality atmosphere and health.* 2016: 9(8): 861-866.

3. The hidden threats lurking in the synthetic fragrances and indoor air fresheners. (Available from https://sfenvironment.org/sites/default/files/fliers/files/sfe_th_air_fresheners_and_dan ger.pdf)
4. Air fresheners and their effect on indoor quality. (Available from <https://www.ambientedge.com/blogs/air-fresheners-and-their-effect-on-indoor-air-quality/>)
5. A Panico et al; Skin safety and Health prevention: An overview of chemicals in cosmetic products, Journal of Preventive Medicine and Hygiene 2019 March; 60 (1): E 50-57.
6. Stacey E Anderson; Potential health effects associated with dermal exposure to occupational chemicals, Environmental Health Insights.2014; 8(Supply 1): 51-62.
7. Make your own natural air freshener (Available from <https://www.motheearthliving.com/green-homes/home-aroma-healthy-all-natural-air-fresheners>)
8. What are the benefits of using air fresheners (Available form <http://juliansherman.net/what-are-the-benefits-of-using-air-fresheners/>)
9. Anne Steinemann; Ten questions concerning air fresheners and indoor built environments, Building and environment, volume 111, Jan 2017, pages 279-284.
10. What are natural air fresheners and what are the advantages (Available from <https://iunatural.com/en/que-son-los-ambientadores-naturales-y-que-ventajas-tienen/>)
11. Natural Home fresheners to make your home smell divine (Available from <https://timesofindia.indiatimes.com/life-style/home-garden/Natural-home-fresheners-to-make-your-home-smell-divine/articleshow/53874115.cms>)
12. Aejaaz A, Azmail, Sanauallah S, Mohsin A.A., Formulation and invitro evaluation of aceclofenac solid dispersion incorporated gels, International Journal of Applied Pharmaceutics,2010, 2(1),8-12
13. A. Cohen, S. Janssen and G. Solomon, "Clearing the Air Hidden Hazards of Air Fresheners," September 2007. NRDC Issue paper.
14. P. Wolkoff and G. D. Nielsen, "Effects by inhalation of abundant fragrances in indoor air – An overview," Environment International., vol. 101, pp. 96–107, 2017.
15. Shivhare UD, Jain KB, Mathur VB, Bhusari KP, Roy AA. Formulation development and evaluation of diclofenac sodium gel using water soluble polyacrylamide polymer Digest Journal of Nanomaterials and Biostructures.2009; 4: 285-290.
16. Jain S, Padsalg BD, Patel AK, Mokale V. Formulation, development and evaluation of Fluconazole gel in various polymer bases. Asian Journal of Pharmaceutics. 2007; 1: 63–8.
17. Niyogi P., Raju N.J., Reddy P.G., Rao B.G. Formulation and evaluation of anti-inflammatory activity of *Solanum Pubescens* Wild extracts gel on albino Wistar rats. International Journal of Pharmaceutics. 2012; 2 (3): 484-490.
18. Goyal S., Sharma P., Ramchandani V, Shrivastava S.K, Dubey P.K. Novel anti-inflammatory topical herbal gels containing *Withania Somnifera* and *Boswellia Serrata*. International Journal of Pharmaceutical and Biological Archive .2011; 2(4): 1087-1094.
19. Mishra U.S., Murthey P.N., Mishra D., Sahu K. Formulation and standardization of herbal gel containing methanolic extract of *Calophyllum Inophyllum*. American Journal of Pharm Tech Research. 2011; 1(1): 276-289.
20. Dixit G., Misal G., gulkari V., Upadhye K. Formulation and evaluation of polyherbal gel for anti-inflammatory activity. International Journal of Pharmaceutical Sciences and Research. 2013; 4(3): 1186-1191.
21. Mishra U.S., Murthy P.N., Pasa G., Nayak R.K. Formulation and evaluation of herbal gel containing methanolic extract of *Ziziphus Xylopyrus*. International Journal of Biological and Pharmaceutical Research. 2011; 1(4): 207-218.
22. Pons R., Solans C., Stebe M., Erra P., Ravey JC 1992, Stability and Rheological properties of gel emulsions; Progress in Colloid and Polymer Science. 89: 110-113.
23. Kumar L, Verma R, In vitro evaluation of topical gel prepared using natural polymer, International Journal of Drug Delivery, 2010, 2, 58-63.
24. Das K, Dang R, Machale UM, Fatepuri S, Formulation and evaluation of herbal gel containing stevia leaves extract, The Pharma Review, 2010, 8(44), 112-118.
25. Prakash RP, Rao R. NG, Soujanya C, Formulation, evaluation and anti-inflammatory activity of topical etoricoxib gel, Asian Journal of pharmaceutical and clinical research, 2010, 3(2), 126-129.
26. Shaik Arif Bhasha, Syed Abdul Khalid, Duraivel S, Debjit Bhowmik and Sampath Kumar KP. Recent trends in usage of polymers in the formulation of dermatological gels. Indian Journal of Research in Pharmacy and Biotechnology. 2013; 1(2):161-168.
27. Praveen S et al; Development and evaluation of antidandruff hair gel. International Journal of Research in Pharmacy and Chemistry 2011; 1(4):936- 949.
28. S Erdogan, EH Zeren, M Emre, O Aydin and D Gumurdulu. Pulmonary effects of deltamethrin inhalation: an experimental study in rats. Ecotoxicology and Environmental Safety. 2006; 63, 318-23.
29. S Patel, AK Pandey, M Bajpayee, D Parmar and A Dhawan. Cypermethrin-induced DNA damage in organs and tissues of the mouse: evidence from the comet assay. Mutation Research 2006; 607, 176-83.
30. IS Richards. The Respiratory System. In: Principles and Practice of Toxicology in Public Health. 1st ed. Jones & Bartlett Publishers, 2007, p. 239-52.
31. P Vineis and K Husgafvel-Pursiainen. Air pollution and cancer: biomarker studies in human populations. Carcinogenesis 2005; 26, 1846-55.
32. M Kale, N Rathore, S John and D Bhatnagar. Lipid peroxidative damage on pyrethroid exposure and alterations in antioxidant status in rat erythrocytes: a possible involvement of reactive oxygen species. Toxicology Letters 1999; 105, 197-205.
33. I Rahman and W MacNee. Oxidative stress and regulation of glutathione in lung inflammation. European Respiratory Society. 2000; 16, 534-54.
34. U Mani, AK Prasad, V Sureshkumar, P Kumar, K Lal, BK Maji and KK Dutta. Hepatotoxic alterations induced by subchronic exposure of rats to formulated fenvalerate (20% EC) by nose only inhalation. Biomed. Environ. Sci. 2004; 17, 309- 14.

Cite this article as:

D. Eswar Tony et al. A comparative study on inhalation toxicology between air fresheners of synthetic and natural origin. Int. Res. J. Pharm. 2020;11(9):9-14. <http://dx.doi.org/10.7897/2230-8407.110977>

Source of support: Nil, Conflict of interest: None Declared

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