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In vitro and *In vivo* Antibacterial and Anti-inflammatory Properties of Linalool

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A B S T R A C T

The present study was planned to determine *in vitro* and *in vivo* antibacterial and anti-inflammatory properties of Linalool. *In vitro* antibacterial activity of Linalool was determined by micro broth dilution technique and MICs were observed as1.25, 1.25, 1.25, 0.63, 1.25, 0.63 and 1.25 mg/ml against *Staphylococcus aureus*, *Streptococcus pyogenus*, *Bacillus subtillis*, *Escherichia coli*, *Salmonella typhimurium*, *Pseudomonas aerugonosa* and *Proteus mirabilis*, respectively. *In vivo* antibacterial efficacy of Linalool was determined in neutropenic rat thigh infection model and significant antibacterial efficacy was observed as compared to growth control with bacterial colony count 4.07 ± 0.05 Log_{10}cfu/ml. *In vitro* anti-inflammatory activity was tested for their ability to inhibit COX-2 enzyme by measuring PGE_2 level and determination of NO production in LPS treated RAW264.7 macrophage cells. At all concentrations of Linalool (10, 50 and 100 µM) found to have significant inhibition of NO and PGE_2 production compared with LPS control group. *In vivo* anti-inflammatory activity of Linalool (100 mg/kg) was assessed using the carrageenan-induced rat paw edema model at different time intervals following intramuscular injection and observed significant percent inhibition of edema volume compared with carrageenan control group.

Introduction

Since ancient era, Indian people have intellectual knowledge of traditional medicine and were used to treat many acute and chronic diseases in human as well as in animal being. Natural sources like plants, animals, microbes are also of great interest in new drug discovery. Furthermore, India has wide diversity in nature which is beneficial to identify newer molecules as therapeutic agent. Phytochemicals like terpenes and terpenoids are used as flavoring agent and play a diverse role in the field of drugs and cosmetics (Perveen, 2018). Linalool is an acyclic monoterpene tertiary alcohol and derived from plants mainly Lamiaceae, Lauraceae and Rutaceae families. Linalool is known to reveal various pharmacological activities such as antimicrobial, anti-inflammatory,

antioxidant and anticancer properties (Kamatou and Viljoen, 2008). Terpenoids are also found in spices and condiments which we are using in our routine life and can be used in primary healthcare. Looking to above facts, present study was planned to evaluate *in vitro* and *in vivo* antibacterial and anti-inflammatory activities of Linalool.

Materials and Methods

Animals

This study was conducted on female albino wistar rats weighing 305 ± 2.60 grams and 353 ± 4.81 grams for *in vivo* anti-inflammatory and antibacterial protocol, respectively. The experimental protocol was approved by Institutional Animal Ethics Committee (IAEC) of Veterinary College, NAU, Navsari with permission number 057-VCN-VPT-2018.

Reagents

Linalool (97%), Lambda (λ) carrageenan, Nω-Nitro-L-arginine methyl ester hydrochloride (NAME), Dulbecco's Modified Eagle's Medium – high glucose (DMEM), Meloxicam, Lipopolysaccharide (LPS), Cyclophosphamide, Iodonitrotetrazolium chloride (INT) and 3-(4,5-dimethylthiazol-2yl)-2,5-diphenyl-2H-tetrazolium bromide (MTT) were purchased from Sigma-Aldrich, St. Louis, USA.

Indomethacin was obtained from Calbiochem. Dimethylsulfoxide (DMSO) andSodium nitrite were purchased from Merck Specialties Private Limited, Mumbai. Chloramphenicol, Celecoxib, Sulfanilamide, N-(1-Naphthyl) ethylenediaminedihydrochloride (NEDD), Eosin Methylene Blue (EMB) agar, Fetal bovine serum, Brain heart infusion (BHI) broth and antibiotic antimycotic solution 100X liquid were purchased from Himedia Laboratories Private Limited, Mumbai. Typed bacterial cultures were purchased from National Collection of Industrial Microorganisms (NCIM), Pune and murine macrophage cell line RAW 264.7 was purchased from National Centre for Cell Science (NCCS), Pune. Ethanol was used from store of Veterinary College, NAU, Navsari after triple distillation. HPLC grade de-ionized water was used in all *in vitro* and *in vivo* procedures.

Prostaglandin E_2 express ELISA kit (Item No. 500141) was purchased from Cayman Chemical Company, Ann Arbor, MI USA.

In vitro antibacterial effect

Linalool stock (40 mg/ml) was prepared in 3% Tween-20. Chloramphenicol stock (250 µg/ml) was prepared in sterile water to use as positive control. Bacterial cultures were prepared to Mcfarland 0.5 standard equivalent to 1.5 x 10^8cfu/ml. Final dispensing inoculums were prepared in sterile test tubes by adding 2 ml bacterial suspension (1.5 x 10^8cfu/ml) of respective organisms into 198 ml of sterile broth. Final dispensing inoculums concentration was 1.5 x 10^6cfu/ml.

Minimum inhibitory concentrations (MICs) of Linalool were determined for different gram positive and gram negative organisms like *Staphylococcus aureus* (ATCC25923), *Streptococcus pyogenus* (ATCC8668), *Bacillus subtillis* (ATCC9372), *Escherichia coli* (ATCC25922), *Salmonella typhimurium* (ATCC23564), *Pseudomonas aerugonosa* (ATCC27853) and *Proteus mirabilis* (NCIM2241) by microbroth dilution technique (Wiegand *et al.*, 2008; Modi *et al.*, 2018). Iodonitrotetrazolium chloride (INT) dye was used to observe visual viability of bacteria. The assay was performed in triplicate.

In vivo antibacterial efficacy

In vivo antibacterial efficacy of Linalool was evaluated in neutropenic rat thigh infection model (Zhao *et al.,* 2016). Neutropenic rat model was prepared by injecting cyclophosphamide intraperitoneally in rats on days 1 (150 mg/kg) and on day 4 (100 mg/kg). After confirmation of neutropenic condition, rats were infected with 0.2 ml bacterial suspension of *Escherichia coli* ATCC25922 (1.5 x 10^8cfu/ml) in left thigh on same day. Linalool (100 mg/kg) which was prepared in DMSO was administered intramuscularly at total injectable volume of 200µl at 2 h and 8 h post infection in right thigh (Group-I). Group-II animals were treated with bacterial suspension (0.2 ml, IM) and Chloramphenicol (50 mg/kg, IM) (Positive Control), Group-III animals were treated with bacterial suspension (0.2 ml, IM) and DMSO (0.2 ml, IM) (Vehicle Control), Group-IV animals were treated with only bacterial suspension (0.2 ml, IM) (Growth Control). After 24 hours, 1 gram thigh muscle samples from infected site were collected following euthanasia under sterile condition. Suitable dilution of samples were inoculated on Eosin Methylene Blue (EMB) agar plates and incubated overnight at 37°C. Bacterial colonies were enumerated by colony counter and $\log_{10}$cfu/gram was calculated.

In vitro anti-inflammatory effect

In vitro anti-inflammatory effect of Linalool was evaluated in murine macrophage cell line RAW 264.7 by measuring COX-2 enzyme inhibition via detection of PGE_2 concentration and by measuring NO production inhibition. Linalool (100 µM, 50 µM and 10 µM) was prepared in 0.008% ethanol in cell culture medium. Cells were grown in DMEM (Dulbecco's Modified Eagle Medium) high glucose supplemented with 10% foetal bovine serum, 1% antibiotic antimycotic solution 100X. The cells were transferred in 12 well plate (1 x 10^6 cells per well) and incubated for 24 hours at 37°C and 5% CO_2 in humidified condition. The cells again washed and supplemented with 1600 µL fresh cell culture medium and 200 µL Linalool in different concentrations (100 µM, 50 µM and 10 µM) for NO production inhibition and PGE_2 inhibition assay. Positive control wells in NO production inhibition assay includes 1600 µL fresh cell culture medium and 200 µL Nω-Nitro-L-arginine methyl ester hydrochloride (NAME, 100 µM) and for PGE_2 inhibition assay positive control wells were dispensed with 1600 µL cell culture medium and 200 µL Celecoxib (100 µM). Vehicle control wells were dispensed with 1600 µL cell culture medium and 200 µL 0.008% ethanol and LPS control wells were dispensed with 1800 µL cell culture medium. Assay was performed in triplicate for test drugs and standards. All plates were incubated at 37°C and 5% CO_2 in humidified condition for 2 hours. Then 200 µL LPS (1 µg/ml) was added in all wells and again incubated at 37°C and 5% CO_2 in humidified condition for 24 hours. After incubation, supernatant was collected in sterile microcentrifuge tubes individually and centrifuged at 3000 rpm for 5 minutes. Supernatant was collected and divided in two parts: one was used to quantify COX-2 enzyme via measuring PGE_2 concentration using Prostaglandin E_2 express ELISA kit from Cayman Chemical Company, Ann Arbor, MI USA following procedure as recommended by the manufacturer (Barton *et al.,* 2014) and another part was used to quantify nitrite accumulated in medium as an indicator of NO production using Griess reaction (Choi *et al.,* 2018). Sodium nitrite standard calibration curve (1.56 µM to 50.0 µM) was prepared to validate the method of estimation and using correlation equation, concentration of NO was evaluated. Results were expressed as percent inhibition of NO and PGE_2 production in comparison to LPS control.

Cell viability

Cell viability was also carried out in test samples by MTT assay (Choi *et al.*, 2018).After sample collection for assay, twenty µL of MTT solution (5 mg/ml) was added to each well, and the plates were incubated for 4 h at 37°C. The supernatants were then collected and the formed formazan crystals in each well were dissolved in 200 µL of dimethyl sulfoxide (DMSO) for 30 minutes at 37°C. The optical density at 570 nm was read in spectrophotometer. Cell viability percentage was calculated.

In vivo anti-inflammatory efficacy

The carrageenan-induced rat paw edema model was used with minor modification as described by (Suebsasana*et al.*, 2009; Modi *et al.*, 2019). Linalool (100 mg/kg) and Indomethacin (5 mg/kg) were prepared in DMSO. Experiment animals (n=24) were divided into 4 groups with 6 animals in each group. A mark on the left hind paw was made in each animal and initial volume was measured by immersing in the plethysmometerpersplex tube. Group-I animals were kept as Carrageenan control. Group-II animals were given DMSO (Vehicle Control), Group-III animals were treated with Indomethacin (5 mg/kg IM) and Group-IV animals were treated with Linalool (100 mg/kg IM). Lambda carrageenan solution (1%) prepared in 0.9% normal saline and 100 µl was injected subcutaneously into sub plantar region of left hind paw. Half an hour before the carrageenan administration, test drug and positive control drug were injected via intramuscular route in respective animal groups. Oedema was measured in paw volume (ml) before carageenan administration and at 1, 2, 3, 4, 5 and 6 h after carrageenan administration and expressed as percent oedema formation in relation to initial paw volume before carrageenan injection for each animal. The paw volume data for test drug and positive control drug were analyzed and expressed as percent inhibition of oedema formation in comparison to carrageenan control group.

Statistical analysis

Data are expressed as Mean ± S.E. The data were analysed using one way ANOVA and significance level was checked at 1 per cent and 5 per cent by Duncan's New Multiple Range Test (DNMRT) using SPSS-20 software.

Results and Discussion

Antibacterial effect

Minimum inhibitory concentration of Linalool against *Staphylococcus aureus, Streptococcus pyogenus, Bacillus subtillis, Escherichia coli, Salmonella typhimurium, Pseudomonas aerugonosa*and *Proteus mirabilis* were observed as 1.25, 1.25, 1.25, 0.63, 1.25, 0.63 and 1.25 mg/ml (Table 1). Significant *in vivo* antibacterial efficacy of Linalool was observed using neutropenic rat thigh infection model with *Escherichia coli* colony count as 4.07 ± 0.05 Log_{10}cfu/ml (Table 2).

Anti-inflammatory Effect

In present study, percent inhibitions of NO production were measured as 37.47 ± 3.30 %, 55.51 ± 2.84 % and 63.07 ± 1.84 % and percent inhibition of PGE_2 production observed as 93.31 ± 0.42 %, 94.34 ± 0.89 % and 94.35 ± 0.29 % at concentrations of 10, 50 and 100 µM, respectively with significant difference at all concentrations in comparison to LPS control (Table 3). Cell viability percentages of cells treated Linalool and other standards including LPS control were compared with blank control and found more

than 96 % viability in all. In present *in vivo* experiment, percent increase in edema volume (8.36 ± 3.94 %, 36.29 ± 4.86 %, 35.22 ± 4.76 %, 36.04 ± 4.32 %, 36.88 ± 5.34 % and 32.82 ± 4.88 %) were significantly lower in comparison with carrageenan control group following administration of Linalool at 1, 2, 3, 4, 5, and 6 hours, respectively (Figure 1). In addition, following intramuscular administration of Linalool, significant percent increase in paw volume percent inhibitions were observed from 3 to 6 hours (Table 4).

Table.1 Minimum Inhibitory Concentrations of Linalool against various gram positive and gram negative organisms

Minimum Inhibitory Concentrations				
Organism	**Linalool (mg/ml)**			
	1	**2**	**3**	**Mode**
***Staphylococcus aureus* ATCC25923**	1.25	1.25	1.25	1.25
***Streptococcus pyogenes* ATCC8668**	1.25	0.63	1.25	1.25
***Bacillus subtilis* ATCC9372**	1.25	1.25	1.25	1.25
***Escherichia coli* ATCC25922**	0.63	0.63	0.63	0.63
***Salmonella typhimurium* ATCC23564**	1.25	1.25	1.25	1.25
***Pseudomonas aeruginosa* ATCC27853**	0.63	1.25	0.63	0.63
***Proteus mirabilis* NCIM2241**	1.25	1.25	1.25	1.25

Table.2 Log_{10}cfu/ml of *Escherichia coli* ($1.5x10^8$cfu/ml) in infected thigh samples of rats treated with drugs including control groups (n=6)

Treatment groups	**Bacterial colony count (Log_{10}cfu/ml)**						**Mean ± S.E.**
	Rat number						
	R1	**R2**	**R3**	**R4**	**R5**	**R6**	
Growth control	5.40	5.28	5.44	5.20	5.32	5.42	5.35 ± 0.03^a
Vehicle control	5.44	5.23	5.39	5.28	5.36	5.33	5.34 ± 0.03^a
Chloramphenicol	4.08	3.90	4.18	3.95	4.15	4.00	4.05 ± 0.04^b
Linalool	4.18	3.90	4.11	4.04	4.20	3.90	4.07 ± 0.05^b

Means bearing different superscripts between treatment groups differ significantly ($p<0.01$)

Table.3 *In vitro* percentage inhibition of NO and PGE_2 production in LPS induced RAW 264.7 cells treated with different concentrations of Linalool

Treatment group	**Percent inhibition (%)± S.E. of NO production**	**Percent inhibition (%)± S.E. of PGE_2 production**
Positive Control	75.72 ± 2.52^b	99.72 ± 0.04^b
Vehicle Control	6.52 ± 1.50^a	3.59 ± 1.33^a
Linalool (10 µM)	37.47 ± 3.30^c	93.31 ± 0.42^c
Linalool (50 µM)	55.51 ± 2.84^d	94.34 ± 0.89^c
Linalool (100 µM)	63.07 ± 1.84^d	94.35 ± 0.29^c

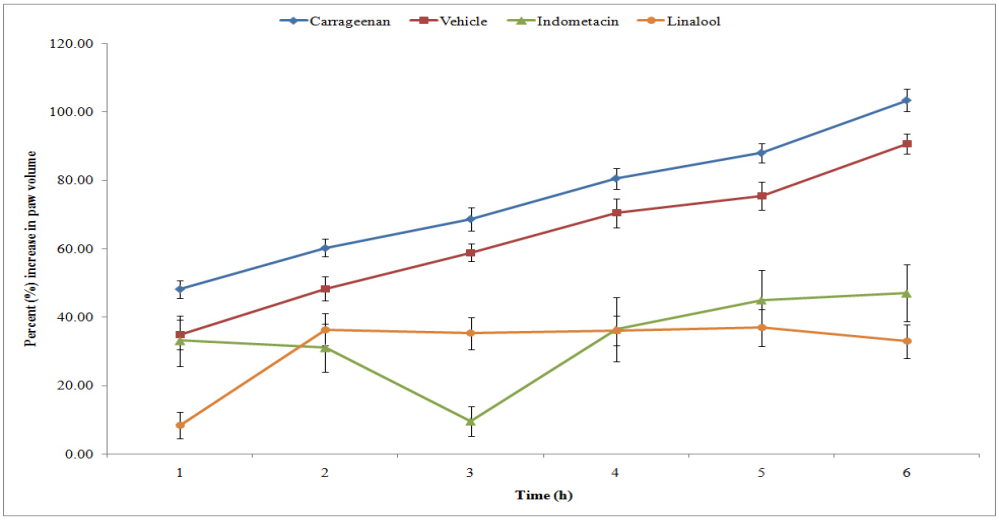
Means bearing different superscripts between treatment groups differ significantly ($p<0.01$)

Table.4 Percent increase (%) in paw volumes (Mean ± S.E.) of carrageenan induced inflammation in rats treated with drugs compared with 0 hour (n=6)

Group	1 Hour	2 Hours	3 Hours	4 Hours	5 Hours	6 Hours
Carrageenan	48.18± 2.62^{aA}	60.21± 2.58^{aB}	68.68± 3.38^{aB}	80.57± 3.04^{aC}	88.01± 2.82^{aC}	103.39± 3.27^{aD}
Vehicle	34.86± 4.25^{abA} (27.65±8.83^{abA})	48.27± 3.55^{abB} (19.83± 5.90^{abB})	58.83± 2.56^{aC} (14.34± 3.73^{aC})	70.39± 4.22^{aD} (12.63± 5.24^{aD})	75.42± 4.00^{aD} (14.31± 4.55^{aD})	90.60± 2.89^{aE} (12.37± 2.80^{aE})
Indomethacin	33.09± 7.39^{bA} (31.32±15.35^{bA})	31.03± 7.06^{bcAB} (48.46±1.73^{bcAB})	9.49± 4.35^{bB} (86.18± 6.33^{bB})	36.42± 9.32^{bcA} (54.80± 11.57^{bcA})	44.97± 8.69^{bA} (48.90± 9.88^{bA})	47.00± 8.31^{bA} (54.54± 8.03^{bA})
Linalool	8.36±3.94^{cA} (82.65±8.18^{cA})	36.29± 4.86^{bcB} (39.73± 7.77^{bcB})	35.22± 4.76^{cB} (48.72± 6.94^{cB})	36.04± 4.32^{bcB} (55.27± 5.36^{bcB})	36.88± 5.34^{bB} (58.10± 6.07^{bB})	32.82± 4.88^{bcB} (68.26± 4.72^{bcB})

Figures in parenthesis shows percent inhibition (%)± S.E. compared with carrageenan control Means bearing different superscripts in small letters between treatment groups and in capital letters within groups differ significantly ($p<0.01$)

Figure.1 Percent increase (%) in paw volumes (Mean ± S.E.) of carrageenan induced inflammation in rats treated with drugs compared with 0 hour (n=6)



Results of present *in vitro* antibacterial study are in agreement with MICs of Linalool were observed by other researchers as 1.024mg/ml against *Staphylococcus aureus* and *Pseudomonas aerugonosa* (Silva *et al.*, 2015) and against *Escherichia coli* and *Staphylococcus aureus* as 0.77 mg/ml and 1.54 mg/ml, respectively (Jabir *et al.*, 2018). In contrast to present study, lower MICs were observed as 5.0, 4.0, 6.0, 5.0, 7.0 and 6.0 µg/ml against *Staphylococcus aureus, Bacillus subtillis, Escherichia coli, Salmonella typhimurium, Pseudomonas aerugonosa* and *Proteus mirabilis,*

respectively (Sokovic *et al.,* 2010). Similarly, Duman*et al.,* (2010) also observed lower MICs as 0.7, 0.9 and 0.7 µg/ml against *Pseudomonas aerugonosa, Escherichia coli* and *Staphylococcus aureus*, respectively. Furthermore, in present study statistically significant *in vivo* antibacterial efficacy of Linalool was observed as compared to growth control in neutropenic rat thigh infection (*Escherichia coli*) model with bacterial colony count 4.07 ± 0.05 Log_{10}cfu/ml which was in agreement with present *in vitro* observations.

Statistically significant and dose dependent percent inhibitions of NO production was observed with Linalool(10, 50 and 100 µM) in present study and significant percent inhibition of PGE_2 production observed at all dose level compared to LPS control. The results observed by other researchers supported results of present study like Peana *et al.,* (2006) examined the effect of Linalool (0.1 µM, 10 µM and 1000 µM) in lipopolysaccharide (LPS) induced macrophages cell line J774.A1 and found significant reduction of NO and PGE_2 production in concentration dependent manner; Li *et al.,* (2015) observed significant and dose dependent inhibition of NO and PGE_2 levels in LPS induced BV2 microglia cells following treatment of Linalool (162, 324, 648 µM) and Kim *et al.,* (2009) evaluated the anti-inflammatory effect of Linalool which is the main content of *Illicium anisatum* extract (25, 50 and 100 mg/ml) in RAW 264.7 macrophage cells and found dose dependent reduction of nitrite and PGE_2 production. In present *in vivo* experiment, significant percent inhibitions of carrageenan induced inflammation were observed following single intramuscular administration of Linalool in comparison with carrageenan control group up to 6 hours. The results of present study are in agreement with percent inhibition observed with Linalool (75 mg/kg) treatment as 38 % and 34 % at 3 and 5 hours after carrageenan administration, respectively (Peana *et al.,* 2002) and percent inhibition of paw edema was observed as 43 ± 9 % and 66 ± 11 % at 4 hours following intraperitoneal administration of Linalool at doses of 50 and 200 mg/kg, respectively in mice (Batista *et al.,* 2010).

In conclusion the linalool possessed *in vitro* antibacterial activity against various gram positive and gram negative organisms with MIC values ranging from 0.63 to 1.25mg/ml. Concurrent, *in vivo* antibacterial efficacy of Linalool was observed in neutropenic rat thigh infection model. Significant decreased NO and PGE_2 levels in LPS induced RAW 264.7 cells treated with different concentrations of Linalool and significant percent inhibition of carrageenan induced rat paw oedema was noticed following single intramuscular administration of Linalool at dose of 100 mg/kg.

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Conflict of interest statement

Authors declare that they have no conflict of interest.

References

Barton, M.H., Paske, E., Norton, N., King, D., Giguere, S. and Budsberg S. 2014. Efficacy of cyclooxygenase inhibition by two commercially available firocoxib products in horses. Equine Vet J. 46(1): 75-75.

Doi:10.1111/evj.12095

Batista, P.A., Werner, M.F.P., Oliveira, E.C., Burgos, L., Pereira, P., Brum, L.F.S., Story, G.M. and Santos, A.R.S. 2010. The antinociceptive effect of (-)-Linalool in models of chronic inflammatory and neuropathic hypersensitivity in mice. The J. of Pain. 11(11): 1222-1229.

Choi, C.W., Shin, J.Y., Seo, C., Hong, S.S., Ahn, E.K., Jung, Y.H. and Oh, J.S. 2018.*In vitro* anti-inflammatory activity of the components of *Amomumtsao-ko* in murine macrophage RAW 264.7 cells.Afr. J. Tradit. Complement. Altern. Med. 15(2): 26-34.

Duman, A.D., Telci, I., Dayisoylu, K.S., Digrak, M., Demirtas, I. and Almae, M.H. 2010. Evaluation of bioactivity of Linalool-rich essential oils from *Ocimum basilucum* and *Coriandrum sativum* varieties. Nat. Prod. Commun. 5(6): 969-974.

Jabir, M.S., Taha, A.A. and Sahib, U.I. 2018.Linalool loaded on glutathione-modified gold nanoparticles: A drug delivery system for a successful antimicrobial therapy. Artif. Cells. Nanomed. Biotechnol. 46(2): 345-355.

Kamatou, G.P.P. and Viljoen, A.M. 2008. Linalool – A review of a biologically active compound of commercial importance. Nat. Prod. Commun. 3(7): 1183-1192.

Kim, J.Y., Kim, S.S., Oh, T.H., Baik, J.S., Song, G., Lee, N.H. and Hyun, C.G. 2009.Chemical composition, antioxidant, anti-elastase, and anti-inflammatory activities of *Illicium anisatum* essential oil. Acta Pharm. 59(3): 289-300.

Li, Y., Lv, O., Zhou, F., Li, Q., Wu, Z. and Zheng, Y. 2015. Linalool inhibits LPS-induced inflammation in BV2 microglia cells by activating Nrf2. Neurochem Res. 40(7): 1520-1525. DOI: 10.1007/s11064-015-1629-7

Modi F.D., Bhavsar S.K., Patel J.H., Varia R.D., Modi L.C. and Kale N. 2018.Evaluation of Pharmacokinetics, Antibacterial and Anti-Inflammatory Activities of Chrysin in Rat. Int.J.Curr.Microbiol.App.Sci. 7(9): 1494-1503.

Modi F.D., Bhavsar S.K., Patel J.H., Varia R.D., Modi L.C., Modi M. and Kale N. 2019. Pharmacokinetic profile of rutin after intramuscular administration in rats favoursits*in vivo* anti-inflammatory activity in carrageenan-induced rodent model of inflammation. Annals of Phytomedicine. 8(1): 185-192.

Peana, A.T., D'Aquila, P.S., Panin, F., Serra, G., Pippia, P. and Maretti, M.D.L. 2002. Anti-inflammatory activity of Linalool and linalyl acetate constituents of essential oils. Phytomedicine. 9(8): 721-726.

Peana, A.T., Marzocco, S., Popolo, A. and Pinto, A. 2006. (-)-Linalool inhibits *in vitro* NO formation: Probable involvement in the antinociceptive activity of this monoterpene compound. Life Sciences. 78(7): 719-723.

Perveen, S. 2018. Introductory Chapter: Terpenes and Terpenoids. Open access peer-reviewed chapter. http://dx.doi.org/10.5772/intechopen.79683

Silva, V.A., Sousa, J.P., Guerra, F.Q.S., Pessoa, H.L.F., Freitas, A.F.R., Alves, L.B.N. and Lima, E.O. 2015. Antibacterial activity of *Ocimum basilicum* essential oil and Linalool on bacterial isolates of clinical importance. Int. J. Pharmacogn. Phytochem. Res. 7(6): 1066-1071.

Sokovic, M., Glamoclija, J., Marin, P.D., Brkic, D. and van Griensven, L.J.L.D. 2010. Antibacterial effects of the

essential oils of commonly consumed medicinal herbs using an *in vitro* model. Molecules. 15(11): 7532-7546.

Suebsasana, S., Pongnaratorn, P., Sattayasai, J., Arkaravichien, T., Tiamkao, S. and Aromdee, C. 2009.Analgesic, antipyretic, anti-Inflammatory and toxic effects of andrographolide derivatives in experimental animals. Arch. Pharm. Res. 32(9): 1191-1200.

Wiegand, I., Hilpert, K. and Hancock, R.E.W. 2008.Agar and broth dilution methods to determine the minimal inhibitory concentration (MIC) of antimicrobial substances. Nature protocols. 3(2): 163-175.

Zhao, M., Lepak, A.J. and Andes, D.R. 2016. Animal models in the pharmacokinetic/pharmacodynamics evaluation of antimicrobial agents. Bioorgan. Med. Chem. 24(24): 6390-6400.

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