

## EVALUATION OF ANTI-INFLAMMATORY EFFECTS OF A POLY HERBAL FORMULATION

Rafeeq Alam Khan\*, Shadab Ahmed and Maryam Aslam

Department of Pharmacology, Faculty of Pharmacy and Pharmaceutical Sciences, University of Karachi,  
Karachi, Pakistan


**ABSTRACT:** Herbal drugs are significant contributors from last thousands of years in providing quality healthcare to humans and still one third of drugs currently in use are directly or indirectly derived from herbal origin. The herbal formulation under investigation includes *Saraca indica*, *Symplocos racemosa*, *Valeriana wallichii*, *Matricaria chamomilla*, *Vitex agnus castus* and *Areca catechu*. This combination is generally used for its marked anti-inflammatory effects in gynecological disorders like menorrhagia, leucorrhea, irregular menstrual cycle, pre-menstrual syndrome and post-menopausal bleeding.

Majority of female population in developing countries are directly exposed to these herbal preparations without any proof of effectiveness hence there was a need to assess its efficacy through scientific methods. Thus it was decided to evaluate the anti-inflammatory activity of the herbal formulation using carrageenan induced hind paw edema technique in albino rats.

Thirty five albino rats of either sex were randomly assigned into five groups with seven animals in each group. Hind paw edema was provoked by sub-planter injection of 0.1 ml of 1% carrageenan, test groups were administered 300, 500 and 1000 mg/kg of herbal formulation suspended in DMSO. Positive control group was given acetyl salicylic acid 300 mg/kg in DMSO and negative control group only received vehicle in equivalent volume. Results of the present study revealed significant anti-inflammatory activity of herbal formulation at 1000 mg/kg in comparison to negative control which was equivalent to positive control.

**Key words:** Anti-inflammatory; Carrageenan; Rat; Hind paw edema

\*Corresponding author: Rafeeq Alam Khan, Department of Pharmacology, Faculty of Pharmacy and Pharmaceutical Sciences, University of Karachi, Karachi, Pakistan, E-mail: [rkhan1959@gmail.com](mailto:rkhan1959@gmail.com)

Copyright: ©2016 Rafeeq Alam Khan. This is an open-access article distributed under the terms of the Creative Commons Attribution License , which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited

## INTRODUCTION

Herbal medicines, sometimes called as botanical medicines, are generally used for their therapeutic or medicinal value for management and cure of different type of ailments. Herbal drugs are significant contributors from last thousands of years in providing quality healthcare to humans and even today herbal medicines are among the most widely used form of drugs in the world (Ekor M, 2014; Gilani AH et al., 2005; Gilani AH et al., 2005; Li TSC, 2002; Lipp FJ, 1996). Now a day's herbal drug are in focus of modern research due to their efficacy shown the treatment and prevention of certain diseases (Barrett B et al., 1999; Ekor M, 2014). These preparations are frequently used all over the world for a variety of disorders including high blood pressure, chronic pain, asthma, hepatitis, common cold, constipation, nervous disorders, allergic rhinitis, diabetes mellitus, gastritis, headache and bowel dysfunction (Luqman S et al., 2014; Terasawa K, 1986).

It is assessed that around one quarter of all recent medications are directly or indirectly obtained from higher plants (Calixto JB, 2000; De Smet PA, 1997; Gurib-Fakim A, 2006). Currently about 122 clinically useful prescription drugs derived from 94 plant species are used worldwide for treatment of human diseases (Cragg GM et al., 2013; Fabricant DS et al., 2001).

Thousands of active principles yet to be discovered or fully evaluated herbal drugs offers a great deal in discovering and synthesizing newer and safer medicines. Various studies have shown that if the right medicinal plants have been taken in appropriate dose and form are as effective as pharmaceutical drugs (Patwardhan B, 2007).

Even though herbal medicines are not devoid of risk (Corns CM, 2003; Ekor M, 2014), but still be safer than synthetic drugs. Regardless of the extensive use and implementation of regularity procedures for herbal medicines, in most cases qualitative and quantitative data are insufficient for final conclusion about the efficacy and safety (Blanka KP et al., 2001). Thus, investigation on herbal drugs might be useful in distinguishing safe and effective herbs from the unsafe or toxic ones.

Inflammation is a transient natural reply of the tissues to injuries that helps in fighting damages caused by exogenous and endogenous agents (Markiewski MM et al., 2007). Inflammatory response tends to remove the stimulus and heals the injured tissue eventually resulting in reconstruction and regaining of homeostasis (Ricciotti E, 2011). It is part of the innate immune response that required activation of specialized cells including leukocytes, neutrophils, eosinophils, basophils, mast cells, monocytes and lymphocytes. Although inflammation is a positive defense mechanism of the body, however several disorders are caused by inflammation that may persist for a long period of time e.g., pain, diabetes mellitus, allergies, atherosclerosis, obesity and cancer. Furthermore, inflammation is the leading cause of chronic diseases (Scriver R et al., 2011).

Large number of plants and their components has been shown to retain analgesic and anti-inflammatory activities (Jamil MSI et al., 2014; Calixto JB et al., 2003). To date usage of most frequently suggested drugs for clinical management of pain and inflammation has been restricted because of probable side effects such as sedation, respiratory depression and dermatological reactions (Rober LJ et al., 2001). Hence more attention has been given on plant based drugs due to their wide biological and medicinal activities, higher safety margins and availability.

The herbal formulation under investigation is indicated for its profound anti-inflammatory effects in gynecological disorders like menorrhagia, leucorrhea, irregular menstrual cycle, pre-menstrual syndrome and post-menopausal bleeding. It is also claimed to strengthen endometrium and ovaries. Herbs present in this combination includes, *Saraca indica*, *Symplocos racemosa*, *Valeriana wallichii*, *Matricaria chamomilla*, *Vitex agnus castus* and *Areca catechu*.

***Saraca indica*** (Caesalpinioideae) is a small evergreen tree indigenous to India. It possess oxytocic activity and used for excessive endometrial bleeding and dysmenorrhea. Its mechanism of action is thought to be direct stimulation of the uterine muscle fibers and stimulation the endometrium and ovarian tissue. It is also believed to have astringent and uterine sedative actions (Pradhan P et al., 2009; Venugopal S, 1998).

***Symplocos racemosa*** (Symplocaceae) is a small tree with dark green leathery leaves. Its bark is considered cooling and mild astringent. It also resolves inflammation and relaxes uterine tissues therefore indicated for menorrhagia. It is recommended for skin and eye infections, hemorrhages and also for bowel complaints, dropsy, liver complaints, fevers, ulcers, scorpion-sting etc (Bhutani KK et al., 2004; Jadhav AN et al., 2005).

***Valeriana wallichii*** (Valerianaceae) is native to Europe and northern Asia and claimed to be powerful nerve stimulant, carminative, antispasmodic, calmative and analeptic agent. *Valeriana wallichii* is a rhizome herb of the genus *Valeriana* and historically been used for restlessness, sleeping disorders, stress, headache, epilepsy, menstrual abnormalities, menopause, stomach cramps, colic and uterine spasticity (Gilani AH et al., 2004; Surajit Sahu et al., 2012).

***Matricaria chamomilla*** (Asteraceae) is a pleasant aromatic plant with a bitter taste. It is principally used in false labor pains, dysmenorrhea, metrorrhagia and leg cramps. It is also claimed to have antispasmodic, expectorant, carminative, anthelmintic, sedative and diuretic properties (Avallone R et al., 1996; Mustafa Cemek et al., 2008).

***Vitex agnus castus*** (Lamiaceae) has been used to treat infertility, amenorrhea and hormonal imbalance in both sexes, and also to prevent pre-menstrual mastodynia. It is a deciduous tree native to the Mediterranean region as far as Western Asia (Christoffel V et al., 1999; van Die MD et al., 2013).

***Areca catechu*** (Arecaceae) is found in the Eastern India and Africa and widely used for cholera, colitis, diarrhea, dysentery, fatigue, fever, gonorrhoea, leucorrhoea, hematuria, herpes, hysteria, malaria, small pox and tapeworm infestation. It has intoxicant, stimulant, astringent, vermifuge and emmenagogue properties as well (Gilani AH et al., 2004; Peng W et al., 2015).

In developing countries like Pakistan, these herbal formulations are freely available in the market for use through self-guidance or untrained advice. There is no regulatory requirement to ensure the efficacy of the product prior to marketing and use. Therefore pharmacological evaluation of such drugs is very important, where large populations are exposed without any scientific proof of efficacy

## MATERIALS AND METHODS

### Selection of Animals

Animals were handled following Helsinki Resolution specifications (1964) and the study was approved by the Board of Advanced Studies and Research University of Karachi. Anti-inflammatory activity study was carried out on 35 Swiss albino Rats of both sex; having 160-210 g body weight. Animals were divided into 5 groups, each comprising of 7 animals. One group served as negative control received vehicle, another group served as positive control received standard drug (acetyl salicylic acid), while remaining three groups served as treated and received different doses of herbal formulation i.e., 300, 500 and 1000 mg/kg.

Animals were preserved at controlled temperature ( $25 \pm 2^\circ\text{C}$ ) and humidity (40-60%) with a 12 hr light /dark cycle. Standard laboratory diet and water was given ad libitum. Before the commencement of anti-inflammatory study, animals were fasted overnight but allowed fresh water prior administering the test materials.

### Composition of Herbal Formulation

Each capsule of the herbal formulation contains herbs in the composition given below

<i>Saraca indica</i>	150 mg
<i>Symplocos racemosa</i>	50 mg
<i>Valeriana wallichii</i>	50 mg
<i>Matricaria chamomilla</i>	50 mg
<i>Vitex agnus castus</i>	50 mg
<i>Areca catechu</i>	50 mg
Talc sufficient to make	500 mg

### Dosing

The herbal formulation in doses of 300, 500 and 1000 mg/kg along with aspirin were prepared in DMSO and administered orally to rats using oral intubation tube. Test and standard drugs were administered 60 minutes prior to induction of paw edema. Aspirin was administered at a dose of 300 mg/kg. Control group only received vehicle in equivalent volume according to body weight.

### Hind paw Edema Method

It is the most commonly used method, based on the measurement of edema in hind paw of rat. The volume of edema can be measured volumetrically with the aid of plethysmography. The substance inducing inflammatory response is called as phlogogenic agent and 0.1 ml of it is generally injected in the sub planter region of hind-paw, the resultant swelling is then measured before and after administration of the test substance, sometime between 30 minutes to 5 hours.

Plethysmometer is a volume meter, particularly designed for accurate measurement of the rat or mouse paw edema. It comprises of water filled Perspex cell into which hind paw is immersed and the transducer records small differences in water level, caused by volume displacement. The digital meter shows the exact volume of water displaced by edema in hind paw; it is probably the most reliable procedure to measure anti-inflammatory effect.

### Determination of paw Edema by Plethysmometer

Anti-inflammatory effect was studied in Swiss albino rats of both sexes, using the method of (Winters WD et al, 1988). Edema was induced in the right hind foot of rats by injecting 0.1 ml of 1% w/v Carrageenan (Sigma Aldrich) suspension prepared in 0.9% saline under the planter apo-neurosis (Ocete MA et al., 1989). The test groups of rats were given 300, 500 and 1000 mg/kg of herbal formulation, one hour before the carrageenan injection. The animals of negative control group were given the same volume of DMSO and animals of positive control group were given 300 mg/kg aspirin by mouth one hour before carrageenan injection.

The paw edema was recorded using plethysmometer (UGO basile Italy). The inflammation was quantified in terms of ml of edema at different time intervals i.e., paw size before administration of carrageenan (time 0=baseline), paw edema immediately after administration of carrageenan, then after 1, 2, 3, 4 and 5 hours respectively for each rat.

The percent inhibition of edema was calculated for each group with respect to its vehicle-treated control group. The anti-inflammatory effect was measured in terms of % inhibition (Palanichamy S et al., 1990).

$$\% \text{ inhibition} = \frac{A-B}{A} \times 100$$

Where A and B represent mean paw volume of control animals and drug treated (standard and test group) animals respectively.

## STATISTICS

Values for anti-inflammatory effect were stated as mean increase in paw volume  $\pm$  S.E.M in terms of milliliters. The significance of difference was measured by Dunnett's t-test and values of  $p < 0.05$  were considered significant and  $p < 0.01$  as highly significant. All statistical procedures were performed according to the method of Alcaraz and Jimenez (Alcaraz MJ et al., 1989).

## RESULTS

The results of anti-inflammatory effects of herbal formulation are depicted in Table 1. The table shows the mean values of the paw volumes at regular intervals (before and after induction of edema by carrageenan injection), mean increase in paw volumes at regular intervals and percentage inhibition of edema after treatment with the herbal formulation, standard drug (positive control) or the solvent DMSO (negative control).

As shown in Table 1, anti-inflammatory activity of herbal formulation was insignificant at 300 and 500 mg/kg; however it was significant at 1000 mg/kg. At 1000 mg/kg, percentage inhibition of edema was 38.7% at 1 hour, 58.7% at 2 hours, 59.9% at 3 hours, 68.2% at 4 hours and 67.4% at 5 hours as compared to the standard drug Aspirin, where percentage inhibition of edema was 41.1%, 60.6%, 67.1%, 73.2% and 79.2% at 1, 2, 3, 4 and 5 hours respectively.

**Table 1: Anti-inflammatory Activity of Herbal Formulation on Carrageenan Induced Rat Paw Edema.**

Treatment	Mean paw volume (ml) $\pm$ S.E.M						Mean increase in paw volume (ml) $\pm$ S.E.M					Percent inhibition of edema $\pm$ S.E.M				
	Before Carrag. Inj.	+1h	+2h	+3h	+4h	+5h	+1h	+2h	+3h	+4h	+5h	+1h	+2h	+3h	+4h	+5h
<b>Control (DMSO)</b>	2.78	3.48	4.10	4.36	4.56	4.68	0.70	1.32	1.58	1.78	1.90					
	$\pm 0.14$	$\pm 0.08$	$\pm 0.13$	$\pm 0.83$	$\pm 0.09$	$\pm 0.10$	$\pm 0.15$	$\pm 0.17$	$\pm 0.16$	$\pm 0.16$	$\pm 0.16$					
<b>Aspirin (300 mg/kg)</b>	2.86	3.27*	3.38*	3.38*	3.34*	3.26*	0.41*	$\pm 0.52^*$	0.52*	0.48*	0.40*	41.1%	60.6%	67.1%	73.2%	79.2%
	$\pm 0.13$	$\pm 0.11$	$\pm 0.10$	$\pm 0.08$	$\pm 0.11$	$\pm 0.11$	$\pm 0.08$	$\pm 0.09$	$\pm 0.09$	$\pm 0.06$	$\pm 0.04$	$\pm 0.16$	$\pm 0.08$	$\pm 0.05$	$\pm 0.04$	$\pm 0.03$
<b>Herbal drug (300 mg/kg)</b>	2.74	3.30	3.65	3.88	4.11	4.34	0.56	0.91	1.14	1.37	1.60	20.2%	31.4%	28.4%	23.0%	15.9%
	$\pm 0.13$	$\pm 0.12$	$\pm 0.17$	$\pm 0.15$	$\pm 0.15$	$\pm 0.13$	$\pm 0.09$	$\pm 0.12$	$\pm 0.10$	$\pm 0.13$	$\pm 0.12$	$\pm 0.57$	$\pm 0.12$	$\pm 0.11$	$\pm 0.09$	$\pm 0.09$
<b>Herbal drug (500 mg/kg)</b>	2.50	3.05	3.33	3.59	3.70	3.62	0.55	0.83	1.09	1.20	1.12	21.8%	37.1%	31.6%	32.4%	41.2%
	$\pm 0.10$	$\pm 0.11$	$\pm 0.09$	$\pm 0.10$	$\pm 0.11$	$\pm 0.14$	$\pm 0.07$	$\pm 0.06$	$\pm 0.10$	$\pm 0.12$	$\pm 0.10$	$\pm 0.26$	$\pm 0.10$	$\pm 0.10$	$\pm 0.08$	$\pm 0.09$
<b>Herbal drug (1000 mg/kg)</b>	2.66	3.09*	3.20*	3.29*	3.22*	3.28*	0.43*	0.54*	0.63*	0.56*	0.62*	38.7%	58.7%	59.9%	68.2%	67.4%
	$\pm 0.12$	$\pm 0.15$	$\pm 0.15$	$\pm 0.15$	$\pm 0.11$	$\pm 0.10$	$\pm 0.13$	$\pm 0.13$	$\pm 0.15$	$\pm 0.06$	$\pm 0.06$	$\pm 0.17$	$\pm 0.09$	$\pm 0.07$	$\pm 0.05$	$\pm 0.04$

n=7; Average value  $\pm$  S.E.M; \* $p < 0.05$  significant as compared to control

## DISCUSSION

Herbal medicine is the oldest form of healthcare and had been used by all cultures throughout history. The WHO has assessed that 80% of the world's population uses traditional therapies (Winters WD et al., 1988; World Health Organization, 1991) a major part of which is plant derived, as their primary health care tools (Akerele O, 1993; Luqman S et al., 2014).

Drug designing is a very pronounced concept used in therapeutic disciplines. Its usefulness lies in its innovative approach towards the development of potent, safe and effective compound of biological interest. Taking into consideration all parameters that form the basis of drug designing, a variety of potent anti-inflammatory compounds has been prepared in the past. Salicylic acid was the first non-steroidal anti-inflammatory agent and then mefenamic acid, Ibuprofen and Indomethacin were introduced (Dudhatra GB et al., 2012; Vane J, 1987).

The major problems encountered by these agents are their toxic tendencies. Owing, to this reason, there was a need to develop some new anti-inflammatory agents with low toxicity profiles and better efficacy. Herbs can prove to be a good source for such compounds (Mueller M et al., 2010). In the present study attempt has been made to confirm the anti-inflammatory activity of the herbal formulation using, acetylsalicylic acid as a standard drug, since it is prototype NSAID and known to have marked anti-inflammatory activity. Some individual herbs present in herbal formulation under investigation have also previously shown to possess anti-inflammatory activity (Subhan F et al., 2007).

Herbal formulation under investigation was first tested for acute and sub chronic toxicities (Gilani AH et al., 2005). Results of present study clearly showed significant inhibitory effect on carrageenan-induced hind paw edema, at 1000 mg/kg dose, while at 300 and 500 mg/kg drug showed modest effects on inhibition of edema. According to the observations, this anti-inflammatory effect was dose-related and was comparable to that of aspirin. The results reported in this study may suggest that herbal formulations may have inhibitory effect on arachidonic acid metabolism by cyclooxygenase pathway since inhibited carrageenan induced inflammation in rat paw. These findings point to a new aspect of pharmacological action of this compound like inhibition of arachidonic acid pathways *in vivo*, so that may exert anti-inflammatory activity where arachidonic acid metabolites are implicated (Ferrándiz ML et al., 1991).

In conclusion, the present data indicates that the said herbal formulation possesses anti-inflammatory potential especially when given in high doses however a decisive conclusion will require further studies on large number of animals followed by clinical studies to establish the efficacy of this formulation in humans.

## ACKNOWLEDGMENTS

This investigation was supported by Herbion Pakistan Private limited.

## REFERENCES

- Akerele O (1993). Summary of WHO guidelines for the assessment of herbal medicines. Herbal Gram 28: 13-19.
- Alcaraz MJ, Jimenez MJ, Valverde S, Sanz J, Rabanal RM, (1989). Anti-inflammatory compounds from *Sideritis javalambrensis* n-hexane extract. J Nat Prod 52: 1088-1091.
- Avallone R, Zanoli P, Corsi L, Cannazza G, Baraldi M (1996). Benzodiazepine-like compounds and GABA in flower heads of *Matricaria chamomilla*. Phytother Res 10: S177-S179.
- Barrett B, Kiefer D, Rabago D (1999). Assessing the risks and benefits of herbal medicine: an overview of scientific evidence. Altern Ther Health Med 5: 40-49.
- Bhutani KK, Jadhav AN, Kalia V (2004). Effect of *Symplocos racemosa* Roxb. on gonadotropin release in immature female rats and ovarian histology. J Ethnopharmacol 94: 197-200.
- Blanka KP, Barbara R (2001). Use of herbal medicines. Ljubljana polje urad Republike Slovenije Zdrauila, Ministrstro Za Zdrauje, Kersnikova ul. 2, 1000 Ljubljana, ZDRAV VESTN 70: 741-806.
- Calixto JB (2000). Efficacy, safety, quality control, marketing and regulatory guidelines for herbal medicines (phytotherapeutic agents). See comment in PubMed Commons below Braz J Med Biol Res 33: 179-189.
- Mustafa Cemek, Sadık Kağa, Nejdet Şimşek, Mehmet Emin Büyükokuroğlu, Muhsin Konuk (2008). Antihyperglycemic and antioxidative potential of *Matricaria chamomilla* L. in streptozotocin-induced diabetic rats. J Nat Med 62: 284-293.

- Christoffel V, Spengler B, Jarry H, Wuttke W (1999). Prolactin inhibiting dopaminergic activity of diterpenes from *Vitex agnus castus*. In *Phytopharmaka V*. Steinkopff. Springer-Verlag Berlin Heidelberg: 209-214.
- Corns CM (2003). Herbal remedies and clinical biochemistry. *Ann Clin Biochem* 40: 489-507.
- Cragg GM, Newman DJ (2013). Natural products: a continuing source of novel drug leads. *Biochim Biophys Acta* 1830: 3670-3695.
- De Smet PA (1997). The role of plant-derived drugs and herbal medicines in healthcare. *Drugs* 54: 801-840.
- Ekor M (2014). The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. *Front Pharmacol* 4: 177.
- Fabricant DS, Farnsworth NR (2001). The value of plants used in traditional medicine for drug discovery. *Environ Health Perspect* 109 Suppl 1: 69-75.
- Ferrándiz ML, Alcaraz MJ (1991). Anti-inflammatory activity and inhibition of arachidonic acid metabolism by flavonoids. *Agents Actions* 32: 283-288.
- Gilani AH, Ghayur MN, Saify ZS, Ahmed SP, Choudhary MI, (2004). Presence of cholinomimetic and acetylcholinesterase inhibitory constituents in betel nut. *Life Sci* 75: 2377-2389.
- Gilani AH, Khan AU, Jabeen Q, Subhan F, Ghafar R (2005). Antispasmodic and blood pressure lowering effects of *Valeriana wallichii* are mediated through K<sup>+</sup> channel activation. *J Ethnopharmacol* 100: 347-352.
- Gilani AH, Rahman AU (2005). Trends in ethnopharmacology. *J Ethnopharmacol* 100: 43-49.
- Gurib-Fakim A (2006). Medicinal plants: traditions of yesterday and drugs of tomorrow. *Mol Aspects Med* 27: 1-9.
- Jadhav AN, Bhutani KK (2005). Ayurveda and gynecological disorders. *J Ethnopharmacol* 97: 151-159.
- Jamil MSI, Sultana Z, Ali ME, Begum MM, Haque MM (2014). Evaluation of Analgesic and Anti-Inflammatory Activities on ethanolic extract of *Terminalia chebula* fruits in experimental animal models. *American Journal of Plant Sciences* 5: 63-69.
- Khan RA, Aslam M, Ahmed S (2016). Evaluation of Toxicological Profile of a Polyherbal Formulation. *Pharmacology & Pharmacy* 7: 56-63.
- Dudhatra GB, Mody SK, Awale MM, Patel HB, CM. (2012). A comprehensive review on pharmacotherapeutics of herbal bio enhancers. *Scientific World Journal* 2012: 637953.
- Rober LJ, Morrow JD (2001). "Analgesic-Anti-Inflammatory Agent and Drugs Employed in the Treatment of Gout," Goodman and Gilman's the Pharmacological Basis of Therapeutics. Mc Graw Hill Companies, America: 696.
- Li TSC (2002). Medicinal plants. Agriculture and food Canada, Pacific agriculture food research center, Summerland, British Columbia: 3-11.
- Lipp FJ (1996). The efficacy, history, and politics of medicinal plants. *Altern Ther Health Med* 2: 36-41.
- Luqman S, Rizvi SI, Beer AM, Khare SK, Atukeren P (2014). Efficacy of herbal drugs in human diseases and disorders. *Evid Based Complement Alternat Med* 2014: 273676.
- Markiewski MM, Lambris JD (2007). The role of complement in inflammatory diseases from behind the scenes into the spotlight. *Am J Pathol* 171: 715-727.
- Mueller M, Hobiger S, Jungbauer A (2010). Anti-inflammatory activity of extracts from fruits, herbs and spices. *Food Chemistry* 122: 987-996.
- Ocete MA, Risco S, Zarzuelo A, Jimenez J (1989). Pharmacological activity of the essential oil of *Bupleurum gibraltaricum*: anti-inflammatory activity and effects on isolated rat uteri. *J Ethnopharmacol* 25: 305-313.
- Palanichamy S, Nagarajan S (1990). Anti-inflammatory activity of *Cassia alata* leaf extract and kaempferol 3-O-sophoroside. *Fitoterapia* 61: 44-47.
- Patwardhan B (2007). *Drug Discovery & Development: Traditional Medicine and Ethnopharmacology*. New India Publishing.
- Peng W, Liu YJ, Wu N, Sun T, He XY, et al. (2015). Areca catechu L. (Arecaceae): a review of its traditional uses, botany, phytochemistry, pharmacology and toxicology. *J Ethnopharmacol* 164: 340-356.
- Pradhan P, Joseph L, Gupta V, Chulet R, Arya H, et al. (2009). *Saraca asoca* (Ashoka): a review. *Journal of chemical and pharmaceutical research* 1: 62-71.
- Ricciotti E, FitzGerald GA (2011). Prostaglandins and inflammation. *Arterioscler Thromb Vasc Biol* 31: 986-1000.
- Calixto JB, Otuki MF, Santos AR (2003). Anti-inflammatory compounds of plant origin. Part I. Action on arachidonic acid pathway, nitric oxide and nuclear factor kappa B (NF-kappaB). *Planta Med* 69: 973-983.
- Scrivo R, Vasile M, Bartosiewicz I, Valesini G (2011). Inflammation as "common soil" of the multifactorial diseases. *Autoimmun Rev* 10: 369-374.

- Subhan F, Karim N, Ibrar M (2007). Anti-inflammatory activity of methanolic and aqueous extract of *Valeriana wallichii* DC rhizome. *Pak. J. Pl. Sci* 13: 103-108.
- Surajit Sahu, Koushik Ray, Yogendra Kumar MS, Shilpa Gupta, Hina Kauser, (2012). *Valeriana wallichii* root extract improves sleep quality and modulates brain monoamine level in rats *Phytomedicine* 19: 924-929.
- Terasawa K (1986). The present situation of education and research work on Traditional Chinese Medicine in Japan. In Presentation at the International Symposium on Integration of Traditional and Modern Medicine, Taichung, Republic of China.
- Van Die MD, Burger HG, Teede HJ, Bone KM (2013). *Vitex agnus-castus* extracts for female reproductive disorders: a systematic review of clinical trials. *Planta Med* 79: 562-575.
- Vane J (1987). The evolution of non-steroidal anti-inflammatory drugs and their mechanisms of action. *Drugs* 33 Suppl 1: 18-27.
- Venugopal S (1998). Effect of Eve Care in Oligomenorrhoea. *Antiseptic* 95: 329-330.
- Winters WD, Hance AJ, Cadd GG, Quam DD, Benthuysen JL (1988). Ketamine- and morphine-induced analgesia and catalepsy. I. Tolerance, cross-tolerance, potentiation, residual morphine levels and naloxone action in the rat. *J Pharmacol Exp Ther* 244: 51-57.
- World Health Organization (1991). Guidelines for the Assessment of Herbal Medicines. Programme on Traditional Medicines, Geneva: 1-4.
- World Health Organization (2005). Guidelines for the assessment of herbal medicines. Organisation mondiale de la santé. WHO global atlas of traditional, complementary and alternative medicine. World Health Organization.

ISSN : 0976-4550

# INTERNATIONAL JOURNAL OF APPLIED BIOLOGY AND PHARMACEUTICAL TECHNOLOGY



Email : [ijabpt@gmail.com](mailto:ijabpt@gmail.com)

Website: [www.ijabpt.com](http://www.ijabpt.com)