A perceptive study of Phytochemical Screening and Anti-inflammatory activity of *Ficus Lacor* roots

Nandani Tripathi[1], Ekta Pandey[2], Mudit Gupta[3]
[1]*Research scholar, Department of Chemistry Mansarovar Global University, Bhopal (M.P.)*
[2]*Associate Professor, Department of Basic Science and Humanities, Bundelkhand Institute of Engineering and Technology, Jhansi U.P.)*
[3]*Principal, Lal Bahadur Shastri PG College, Jaipur Rajasthan*

***Abstract*—Object: To perform the Phytochemical Screening & Anti-inflammatory activity of *Ficus Lacor* roots in Albino Wistar rats.**
Methods: The different Pharmacognostical parameters were evaluated as per standard procedure. The crude drug was evaluated for organoleptic properties shape, size, colour, odour, taste. Preliminary Phytochemical Screening was carried out & finally Anti-inflammatory activity was evaluated by adopting different methods. Results: The extracts showed a marked Anti-inflammatory effect. The fraction from *Ficus lacor* aerial roots showed maximum inhibition (80%) of Carrageenan induced edema. The inhibition of inflammation was comparable for all the fractions for any change in extent & percentage of inhibition at 30 min, 1hr, 2hr and 3hr. The anti-inflammatory effect induced via indomethacin gradually increased and reached at higher level (80.8%) after 3 hrs.
Conclusion: The results of the study indicate that the extract of *Ficus lacor* possesses strong Anti-inflammatory activity. This study also describes therapeutic effect of *Ficus lacor* aerial roots in inflammation and arthritis which will give a new direction for the future scientific research.

***Index Terms*—Anti-inflammatory activity, *Ficus lacor*, Inflammation, medicinal plants**

I. INTRODUCTION

Medicinal plants play vital roles in primary healthcare system of various developing countries due to lack of modern healthcare infrastructure, traditional acceptance, high cost of pharmaceutical drugs as well as efficacy of medicinal plants against certain disorders that cannot be treated by modern therapeutic drugs (Megersa and Tamrat, 2022). Numerous patients in these developing countries combine folklore medicines with standard medicines and use them for the treatment of chronic diseases (Kigen et al., 2013). Ficus genuses include trees, hemi-epiphytes, shrubs, creepers, and climbers and are distributed in the forests, tropical and subtropical areas of Asia, Africa, America, and Australia (Hamed, 2011). Certain Indian Ficus species do not bear fruits, but they have similar morphological characters that are problematic to be distinguished from their species and variants. Every part of Ficus plants is used in the treatment of peptic ulcers, piles, jaundice, haemorrhage, diabetes, asthma, diarrhoea, dysentery, biliousness, and leprosy (Khan and Khatoon, 2007). Different species of Indian Ficus genus contain sesquiterpenes, monoterpenes, triterpenoids, phenolic compounds, flavonoids, anthocyanins, alkaloids, furanocoumarins, organic acids, volatile components, and phenylpropanoids (Tamta et al., 2021). These metabolites occur in latex, leaves, fruit, stem, and roots of different species (Shahinuzzaman et al., 2021). The Indian Ficus plants possess remarkable analgesic (Mahajan et al., 2012), antimicrobial (Patil and Patil, 2011), antiarthritic (Thite et al., 2014), anticancer (Abbasi et al., 2017), neuroprotective (Ramakrishna et al., 2014) and antidiabetic properties (Anjum and Tripathi, 2019).

Inflammation is a complex biological process involving several chemical mediators that are induced by the vascular tissue of the body when it comes in contact with harmful stimuli such as pollens, irritants, pathogens and damaged cells. The process of inflammation involves several events and mediators that are potent chemical substances found in the body tissues, such as prostaglandins, leukotrienes, prostacyclins, lymphokines, and chemokines such as interferon-α (IFN-α), γ, interleukin (IL)-1, IL-8, histamine, 5-hydroxytryptamine (5-HT), and tissue necrosis factor-α (Serhan and Savill, 2005). Anti-inflammatory drugs of synthetic origin are classified as steroidal and non-steroidal anti-inflammatory agents. The origin of these chemical compounds started when salicylates were isolated from the leaf extract of willow bark (***Salix alba***) and were used by the people of North America in 200 BC; they are regarded as the first generation of anti-inflammatory agents (Rainsford and Whitehouse 1980). These were followed by the discovery of second- and third-generation compounds with preferential and selective cyclooxygenase (COX_2) inhibitory activities, such as nimesulide, nabumetone, celecoxib, rofecoxib, valdecoxib and etoricoxib. Apart from the non-steroidal drugs, various corticosteroids such as hydrocortisone, betamethasone, and beclomethasone are primarily used as anti-inflammatory agents (Ang-Lee et al., 2001). Some common side effects of these synthetic drugs include gastric irritation, ulceration, bleeding, renal failure, interstitial nephritis, hepatic failure, headache, thrombocytopenia, haemolytic anemia, asthma exacerbation, skin rashes, angioedema and pruritis (Anonymous, 1996). Hence, the approach for treating inflammatory diseases by herbal drugs has the keen interest of researchers. From a global study, it has been seen that the market for herbal drugs in the treatment of inflammatory diseases constitutes 83% worldwide and is expected to reach a value of over 95% in the forthcoming years due to the increased acceptability of these preparations (Bent and Ko, 2004). According to the WHO, about 80% of the world’s population relies on traditional drugs to treat various types of ailments (Sindhu et al., 2010. It is a large deciduous, rapidly growing closely foliaceous tree about 20 m in height with a fine shaped crown. It is widely distributed in tropical and subtropical regions of the world. It grows in various humid regions in India. The bark of the plant in the traditional medicine of India is used for the treatment of ulcers, for expelling roundworms and for the treatment of leucorrhoea. The leaves are also used for treating various skin problems (Gamble, 1922). Phytochemical screening of the plant revealed the presence of terpenoids, sterol, amino acids and flavonoids, etc. Medicinal plants or isolated bioactive constituents form one of the major sources of raw materials for drugs in preventive or curative applications (Jain and Yadav, 1994). The present study was undertaken to evaluate the anti-inflammatory potential of aerial root extracts of *Ficus lacor*.

II. REVIEW OF LITERATURE

Research in the field of photochemistry continues to develop from year to year for the sustainability of human health. Thousands of new compounds have been discovered every year in the development of drugs from natural ingredients, especially plants (Pandey et al., 2013). Plants can create secondary metabolites that can be used as pesticides, fragrances, colours, antioxidants, food enhancers, and medications, including ones that treat hypertension (Ochatt et al., 2022). There are 150,000 secondary metabolites that have been identified and 4000 new secondary metabolites per year. Phytochemicals are natural bioactive compounds that produce physiological actions in the human body, interacting with nutrients and fiber will protect the human body against disease (Kumar et al., 2023). Phytochemicals that are highly significant include alkaloids, flavonoids, tannins, saponins, and phenols. Medicinal plants play vital roles in primary healthcare system of various developing countries due to lack of modern healthcare infrastructure, traditional acceptance, high cost of pharmaceutical drugs as well as efficacy of medicinal plants against certain disorders that cannot be treated by modern therapeutic drugs (Megersa and Tamrat, 2022). Numerous patients in these developing countries combine folklore medicines with standard medicines and use them for the treatment of chronic diseases (Kigen et al., 2013). Ficus genus includes trees, hemi-epiphytes, shrubs, creepers, and climbers and are distributed in the forests, tropical and subtropical areas of Asia, Africa, America, and Australia (Hamed, 2011; Ahmed and Urooj, 2010b). Certain Indian Ficus species do not bear fruits, but they have similar morphological characters that are problematic to be distinguished from their species and variants. Every part of Ficus plants is used in the treatment of peptic ulcers, piles, jaundice, haemorrhage, diabetes, asthma, diarrhoea, dysentery, biliousness, and leprosy (Khan and Khatoon, 2007). Different species of Indian Ficus genus contain sesquiterpenes, monoterpenes, triterpenoids, phenolic compounds, flavonoids, anthocyanins, alkaloids, furanocoumarins, organic acids, volatile components, and phenylpropanoids (Khayam et al., 2019; Shao et al., 2018; Tamta et al., 2021). These metabolites occur in latex, leaves, fruit, stem, and roots of different species (Shahinuzzaman et al., 2021). The Indian Ficus plants possess remarkable analgesic (Mahajan et al., 2012), antimicrobial (Patil and Patil, 2010), antiarthritic (Thite et al., 2014), anticancer (Jamil and Abdul Ghani, 2017), neuroprotective (Ramakrishna et al., 2014) and antidiabetic properties (Anjum and Tripathi, 2019).

2.1 Analgesic activity: -

Pain is a nonspecific expression of various diseases in humans. The non-steroidal anti-inflammatory molecules and opiates have been used traditionally in these conditions, but several adverse effects arise with these drugs such as gastrointestinal disorders, renal injury, and respiratory problems (Domaj et al., 1999). Nowadays, the researchers are showing their interests in searching of novel analgesic compounds from medicinal plants with possibly fewer adverse effects. Aqueous extract (400 mg/kg, p.o.) of *F. bengalensis,* in the early (0-5 min) and late phases (25-30 min) of pain, showed significant reduction in the duration of licking responses in formalin-induced pain model. The responses were compared to morphine-treated animals (P < 0.001 as compared to the control; Rajdev et al., 2018). The hot aqueous extract (500, 1000 and 2000 mg/kg) of *F. carica* fruits did not show any significant difference between control and treated animals (P greater than 0.05), but a significant variability reported in between the petroleum ether extract (1000 mg/kg) and the dimethyl sulfoxide treated animals (P < 0.05; Mirghazanfari et al., 2019). Ethanol extract of ***F. religiosa*** leaves (400 mg/kg b.w.) showed significant increase in latency time (70.81 %; P<0.05) in Eddy's hot plate model when compared to control. Leaf extract (400 mg/kg b.w.) suppresses the number of writhing's (68.47 %), induced by acetic acid, when compared to diclofenac (68.47 %; P < 0.05; Marasini et al., 2020). Ethanol extract of *F. iteophylla* leaves (200 mg/kg) decreases the number of acetic acid-induced abdominal constriction (3.0 ± 0.82) when compared to ketopfofen (reference drug; 10 mg/kg; 4.30 ± 1.28; P < 0.05; Abdulmalik et al., 2011).

2.2 Anti-inflammatory activity: -

Ethanol extract of *F. carica* leaves (600 mg/kg b.w.) demonstrated potent anti-inflammatory activity in acute (75.90%) and chronic (71.66%) inflammations when compared to indomethacin (P < 0.001; Patil and Patil, 2011). Aqueous extract of *F. benjamina* leaves (264 mg/kg b.w.) exhibits higher anti-inflammatory effect (39.71%) than the negative control in experimental animals (70.12%; P < 0.05 Bunga and Fernandez, 2021).

2.3 Antimicrobial activity: -

The microbial drug resistance to widely used antimicrobial drugs has increased the universality of microbial infections and their related problems (Ginovyan et al., 2017). Methanol extract (60 mg/disc) of *F. auriculata* fruits demonstrates strong antimicrobial effect against S. epidermidies (28 mm), and *M. genetalium* (MTCC 2288; 28 mm; Raja et al., 2021). Two compounds (ficuisoflavone and alpinumisoflavone) from F. auriculata fruits exhibit potent antibacterial effect against pathogenic bacteria (*S. aureus, K. pneumoniae, B. cereus, N. gonorrhoeae*, and *P. aeruginosa*; MIC 1.25 to 20 lg/ml; Shao et al., 2022). Four isoflavones (5,7,40-trihydroxy-30-hydroxymethylisofla vone, 30-formyl-5,40-dihydroxy-7-methoxyisoflavone, ficuisoflavone and alpinumisoflavone) from *F. auriculata* roots displays strong antibacterial activity against *S. pneumoniae, S. pyogenes, S. typhi, S. dysenteriae, E. coli* and *V. cholera* (MIC from 1.30 to 39.93 lM; Qi et al., 2018). Methanol extract *F. religiosa* leaves (50 lL/well concentration) exhibited greater activity than aqueous extract against the tested microorganisms (*S. aureus, E. coli, P. aeruginosa, S. typhi, A. niger* and *Penicillium notatum*; Pathania et al., 2021).

2.4 Antioxidant activity: -

Oxidative stress is known as a main reason for the occurrence and continuance of various diseases (Singh et al., 2021). Plants are considered as a rich source of exogenous antioxidants (Singh and Sharma, 2020). Ethanol extract of *F. racemosa* fruits showed strong antioxidant activity on ABTS (EC_{50} 226.0 ± 1.77 mg/mL), FRAP (EC_{50} 234.8 ± 1.72 mg/mL), DPPH (EC_{50} 28.4 ± 0.50 mg/mL) radical scavenging, hydrogen peroxide radical scavenging (EC_{50} 376.7 ± 2.05 mg/ mL), hydroxyl radical scavenging (EC_{50} 427.2 ± 3.06 mg/mL), chelating power (EC_{50} 176.6 ± 3.00 mg/mL), and reducing power (EC_{50} 356.3 ± 4.75 mg/mL) assays (Tamuly et al., 2015).

2.5 Neuroprotective activity: -

Neurodegenerative disorders cause slow neuronal death that led to the loss of cognitive functions and sensory dysfunctions (Mattson et al., 2004). Nowadays, these disorders are linked to various multifactorial pathologies, social, and financial issues. (Methanolic extract *of F. benghalensis* leaves showed potent inhibitory effect to acetylcholine esterase activity (IC50 = 194.6 ± 7.96 1 lg/mL) when compared to donepezil (IC_{50} = 186.1 ± 7.1 lg/mL; Hassan et al., 2020). Ethanol extract of *F. erecta* leaves significantly reduced neuronal loss and neuronal nuclei expression in the brain tissues of Ab injected mice. Extract significantly changed the Ab-induced inhibition of cAMP response element-binding protein phosphorylation and the expression of brain-derived neurotrophic factor, showing mechanism of neuroprotection. Extract significantly suppressed the formation of interleukin-1b and tumour necrosis factor-a, and the ionized calcium-binding adaptor molecule 1 expression in brain tissues of Ab-injected mice, proposing antineuroinflammatory actions.

2.6 Anti-stress activity: -

Stress is a general physiological response of the body focussed on available resources and minimizing the influence on the body of pessimistic aspects (Doreddula et al., 2014). Stress is linked to pathological processes of hypertension, peptic ulcer, immunosuppression, and reproductive complications (Piato et al., 2008). Methanol extract of F. *benghalensis* fruits showed acetylcholinesterase inhibitory effect in SHSY5Y cells lines (IC_{50} 228.3 lg/mL; Vignesh et al., 2019). The methanol extract (500 mg/kg) also displayed dose and duration dependent significant delay in clonic convulsions (51.1 ± 1.4) on anoxia stress tolerance time in mice when compared to positive control (*Withania somnifera*, 100 mg/kg, p.o.; 64.5 ± 2.0; P < 0.001; Jahagirdar et al., 2020).

2.7 Radioprotective activity: -

Radiations can cause mutagenic alterations, and lead to the formation of cancers. Plants that could defend the body from radiation effects would be of great interest (Mamedov et al., 2011). The radioprotective effect of ethanol extract of *F. racemosa* stem bark was tested on electron beam radiation induced-DNA damage. The extract (50 mg) displayed significant inhibition on radiation induced-DNA damage when compared to control (P < 0.001; Vinutha et al., 2015). Ethanol extract of *F. racemosa* (20 lg/mL) showed a significant radioprotection (P < 0.01) to 4 Gy c-irradiation when compared to the radiation controls. The cytokinesis-block proliferative index revealed that extract does not change radiation stimulated cell cycle delay (Veerapur et al., 2009).

III. MATERIALS AND METHODS

3.1 Plant Material: -

The aerial roots of *Ficus lacor* were collected in the month of August from local area. The plant material was taxonomically identified in accordance with the guidelines set forth by botanists Sharma et al., (1993).

3.2 Preparation of extract: -

The aerial roots were extracted with water. The mixture was filtered and evaporated to dryness. The dark brownish powder obtained was stored in a well-closed airtight light resistant container.

3.3 Animals: -

Adult male Albino Wistar rats (150-200 g) were used to study the anti-inflammatory activity. The animals (five per cage) were maintained under standard laboratory conditions (light period of 12 hrs/day and temperature 27° C ± 4° C), with access to food and water ad libitum. The experimental procedures were carried out in strict compliance with the Institutional Animal Ethics Committee regulations. All experiments were performed in the morning according to the guidelines for the care of laboratory animals (Zimmermann, 1983).

3.4 Anti-inflammatory activity: -

Carrageenan induced rat paw oedema The anti-inflammatory activity of *Ficus Lacor* roots was evaluated by carrageenan induced rat paw oedema method (Gopalkrisna et al., 2006; Winter et al., 1962). Male Albino Wistar rats (150-200 g) were randomly distributed into 4 groups of five animals each. First group served as a control, second group served as the standard (received aceclofenac sodium 10 mg/kg, i.p), while the third and fourth group received 100 and 200 mg/kg, body weight of AEFB respectively. After 30 min 0.1 ml of 1 % w/v suspension of carrageenan was injected into the sub plantar region of right hind paw to all the four groups. The paw volumes were measured using plethysmometer, every hour till 3 h after carrageenan injection, and mean increase in paw volumes were noted. Thus, edema volumes in control (Vc) and in groups treated with test compounds (Vt) were calculated. The percentage inhibition was calculated by using the formula (Turner, 1965).

$$\% \, Inhibition = \frac{V_c - V_t}{V_c} X \, 100$$

Where,
Vc = Edema volume of Control,
Vt = Edema volume of Test

3.5 Cotton pellets induced granuloma: -

The granuloma formation induced with cotton pellet as described by Penn and Ashford in 1963. Cotton rolls were cut and made into pellets weighing 10 ± 01 mg each and sterilized with an autoclave at 100°C for 30 min. Under ether anaesthesia, the pellets (rolls) were introduced subcutaneously (s.c.) through skin incisions on both sides in the scapular region of the rats. The daily administration of normal saline, aqueous extract (100 and 200 mg/kg, p.o.) and aceclofenac sodium (10 mg/kg, i.p) as reference standard were started 3 h after cotton pellet implants and continued for 14 days (daily p.o. administration). On the 15th day, the animals were anaesthetized with ether and the granulomas were removed and weighed. The difference between the initial weight of cotton pellet and final weight of the granuloma and the cotton pellet were considered to be the weight of granulomatous tissue produced (Santos et al., 1996).

3.6 Statistical Analysis: -

The statistical analysis of all the results was carried out using one-way ANOVA followed by Dunnet's multiple comparisons test and all the results obtained in the study were compared with the vehicle control group. **p < 0.01 were considered statistically significant.

IV. RESULTS AND DISCUSSION

The results of aqueous extract against carrageenan-induced paw edema and cotton pellet induced granuloma formation in rats are shown in table 1 and 2. Studies demonstrate that various flavonoids such as rutin, quercetin, luteolin, hesperidin and biflavonoids produced significant anti-inflammatory activities (Galati et al., 1994; Rao et al., 1998). There are also few reports on the role of tannins in anti-inflammatory activities (Ramprasath et al., 2006). NSAIDs can inhibit cyclooxygenase in peripheral tissues, thus interfering with the mechanism of transduction in primary afferent nociceptors (Fields, 1987).

Mean Paw Volume (ml) ± S.E.M (0 hr)			
Treatment	Dose (mg/kg)	EV (ml)	EI(%)
Vehicle control	-	0.702 ± 0.019	-
Aceclofenac sodium	10	0.594 ± 0.016**	15.34
Aqueous extract of FL	100	0.417 ± 0.01**	40.59
Aqueous extract of FL	200	0.256 ± 0.007 **	63.53
1 hr			
Vehicle control	-	0.85 ± 0.005	-
Aceclofenac sodium	10	0.464 ± 0.005**	45.41
Aqueous extract of FL	100	0.758 ± 0.005**	10.82
Aqueous extract of FL	200	0.560 ± 0.007**	34.11
2hr			
Vehicle control	-	1.34 ± 0.082	-
Aceclofenac sodium	10	0.077 ± 0.002**	94.25
Aqueous extract of FL	100	0.698 ± 0.053**	47.91
Aqueous extract of FL	200	0.462 ± 0.035**	65.52
3hr			
Vehicle control	-	1.43 ± 0.01	-
Aceclofenac sodium	10	0.008 ± 0.00**	99.44
Aqueous extract of FL	100	0.522 ± 0.00**	63.49
Aqueous extract of FL	200	0.427 ± 0.00**	70.13

Values are mean ± SEM (n=5); **p<0.01 when compared with vehicle control.
Vehicle control received normal saline; FL, Ficus lacor

The mechanism of anti-inflammatory action of aqueous extract of Ficus Lacor could be due to the presence of flavonoids, mediated through central and peripheral mechanisms. Carrageenan induced paw oedema was taken as a prototype of exudative phase of acute inflammation. Inflammatory stimuli microbes, chemicals and necrosed cells activate the different mediator syflowers through a common trigger mechanism. The development of carrageenan induced oedema is believed to be biphasic.

Table 1: - Anti-inflammatory activity of aqueous extract of aerial roots of *Ficus lacor* on carrageenan induced paw oedema in rats

Treatment	Dose (mg/kg)	Weight of cotton pellet- induced granuloma (mg)	Inhibition (%
Vehicle control	-	40.66 ± 1.22	-
Aceclofenac sodium	10	18.33 ± 0.76**	54.91
Aqueous extract of FL	100	27.83 ± 0.47**	31.55
Aqueous extract of FL	200	22 ± 0.51**	45.89

Values are mean ± SEM; n=5., **P<0.01 when compared with vehicle control.

Table 2: - Effects of the aqueous extract of aerial roots of *Ficus laco*r (100 - 200 mg/kg, p.o.) and Aceclofenac sodium (10mg/kg, i.p) on cotton pellet-induced granulomatous tissue formation in rats

The early phase is attributed to the release of histamine and serotonin and the delayed phase is sustained by the leucotrienes and prostaglandins (Vinegar et al., 1976). Flavonoids and tannins are reported to inhibit PG synthesis (Alcaraz and Ferrandiz, 1987). Most of the NSAIDs have well balanced anti-inflammatory and ulcerogenic activities, which are considered to be due to PG synthetase inhibitor activity. Oral administration of the aqueous extract of *Ficus Lacor* over the stated period resulted in a marked dose-dependent anti-inflammatory activity in the cotton pellet-induced granuloma at a dose of 200 mg/kg (table 2). The dry weight of the pellets correlates well with the amount of granulomatous tissue (Swingle and Shideman, 1972). The effect was however, lower than that obtained with aceclofenac sodium (10 mg/kg), a standard non-steroidal anti-inflammatory drug. The sequence of events in the formation of granuloma begins with the presence of an antigen (cotton pellet), which causes stimulation of the immune system, production of antibodies, interleukins and of compliment. With persistent antigenic stimulation, there is proliferation by lymphocytes and formation of inflammatory granulation tissue over the pellets (Ukwe, 1996). The significant decrease in the granuloma formation as observed in the study might be due to the influence of the biologically active substances from the aqueous extract on the sequence of events as described. This effect showed the ability of the extract in reducing the number of fibroblasts, and synthesis of collagen and mucopolysaccharide, which are natural proliferative events of granulation tissue formation. The observed lower effect as compared to Aceclofenac sodium could be due to the crude state of the extract, which means that the active component responsible for the anti-inflammatory activity in the total dose administered is suboptimal. From the above discussion, the aqueous extract of aerial roots of *Ficus Lacor* exhibited significant anti-inflammatory activity. Further detailed investigation is underway to determine the exact phyto-constituents those are responsible for these activities.

BIBLIOGRAPHY

[1] Abbasi, S., Kamalinejad, M., Babaie, D., Shams, S.M., Sadre, Z., Gheysarif, M., Askari, V.R., Rakhshandeh, H., (2017). A new topical treatment of atopic dermatitis in pediatric patients based on Ficus carica L. (Fig): A randomized, placebo-controlled clinical trial. Complement. Ther. Med. 35, 85-91.

[2] Abdullahi, A.A., (2011). Trends and challenges of traditional medicine in Africa. African J. Trad. Complement. Altern. Med. 8, 115-123.

[3] Abdulmalik, I.A., Sule, M.I., Musa, A.M., Yaro, A.H., Abdullahi, M.I., Abdulkadir, M.F., Yusuf, H., 2011. Evaluation of analgesic and anti-inflammatory effects of ethanol extract of Ficus iteophylla leaves in rodents. African J. Tradit. Complement. Altern. Med. 8, 462-466.

[4] Ahmed, F., Urooj, A., (2010). Hepatoprotective effects of Ficus racemosa stem bark against carbon tetrachloride-induced hepatic damage in albino rats. Pharm. Biol. 48, 210-216.

[5] Alcaraz, M.J., Ferrandiz, M.L., (1987). Modification of arachidonic metabolism by flavonoids. Journal of Ethnopharmacology, 21(3): 209-229.

[6] Ang-Lee, M. K., Moss, J., Yuan, C. S., (2001). Herbal medicines and perioperative care. J Am Med Asso. 286,208-16.

[7] Anjum, N., Tripathi, Y.C., (2019). Phytochemical screening and in vitro evaluation of antidiabetic activity of Ficus palmata fruits. European J. Pharm. Med. Res. 6, 251-258.

[8] Anonymous, (1996). Program profile. International liaison brings global vision to OAM. Complementary and Alternative Medicine at the NIH, 3:3-10.

[9] Bent and Ko, R., (2004). Commonly used herbal medicines in the United States: A review. Am J Med. 116,478-85.

[10] Bunga, D.M., Fernandez, S.S.A., (2021). Anti-inflammatory activities of aqueous extract of beringin (Ficus benjamina L.) and kersen (Muntingia calabura L.) leaves in albino rats. J. Katalisator 6, 254-260.

[11] Chopra, R.N., Nayar, S.L., Chopra, I.C., (1956). Ficus Glossary of Indian Medicinal Plants. CSIR, New Delhi.

[12] Cox, A.P., Balick, J.M., (1996). Ethnobotanical research and traditional health care in developing countries, plants, people, and culture. New York, W.H, Freeman Comp.

[13] Domaj, M.I., Glassco, W., Aceto, M.D., Martin, B.R., (1999). Antinociceptive and pharmacological effects of metanicotina, a selective nicotine agonist. J Pharmacol Exp Ther 291, 390-398.

[14] Doreddula SK, Bonam SR, Gaddam DP, Desu BS., (2014). Phytochemical analysis, antioxidant, antistress, and nootropic activities of aqueous and methanolic seed extracts of ladies finger (Abelmoschus esculentus L.) in mice. Sci World J 2014, 519848.

[15] Fields, H.L., (1987). Analgesic Drugs. In: Day W Eds. Pain. 1st edition. Mac Graw-Hill, USA.

[16] Galati, E.M., Monforte, M.T., Kirjavainen, S., Forestieri, A.M., Trovato, A., Tripodo, M.M., (1994). Biological effects of hesperidin, a citrus flavonoid: anti-inflammatory and analgesic activity, Pharmacology, 40(11): 709-712.

[17] Gamble, G. S., (1922). Flora of Presidency of Madras, V. III.1356-1357.

[18] Ginovyan, M., Petrosyan, M., Trchounian, A., (2017). Antimicrobial activity of some plant materials used in Armenian traditional medicine. BMC Complement Alter Med 17, 50.

[19] Gopalkrisna, B., Sutar, P.S., Akki, K.S., Gadad, P.C., Hukkeri, V.I., (2006). Anti-inflammatory activity of different extracts of Stachytarpheta Indica L (VAHL) leaves. Indian Drugs, 43: 255-57.

[20] Hamed, M.A., (2011). Beneficial effect of Ficus religiosa Linn. on highfat- diet-induced hypercholesterolemia in rats. Food Chem 129, 162-170.

[21] Hassan, H.A., Allam, A.E., Abu-Baih, D.H., Mohamed, M.F.A., Abdelmohsen, U.R., Shimizu, K., Desoukey, S.Y., Hayallah, A. M., Mahmoud, A., Elrehany, M.A., Mohamed, K.M., Kamel, M. S., (2020). Isolation and characterization of novel acetylcholinesterase inhibitors from Ficus benghalensis L. leaves. RSC Adv 10, 36920 -36929.

[22] Jahagirdar, M.A.Q.F., Hugar, S., Patil, V.P., Anant, K., Nanjappaiah, H.M., (2020). Screening of anti-stress activity of Ficus benghalensis fruit extract. Res J Pharm Technol 13, 191-196.

[23] Jain, N., Yadav, R. N., (1994). Fitoterapia. 65, 94-96.

[24] Khan, S.W., Khatoon, S., (2007). Ethnobotanical studies on useful trees and shrubs of Haramosh and Bugrote valleys, in Gilgit Northern areas of Pakistan. Pak J Bot 39, 699-710.

[25] Khan, S.W., Khatoon, S., (2007). Ethnobotanical studies on useful trees and shrubs of Haramosh and Bugrote valleys, in Gilgit Northern areas of Pakistan. Pak J Bot 39, 699-710.

[26] Khayam, S.M.U., Zahoor, M., Shah, A.B., (2019). Biological and phytochemical evaluation of Cotoneaster microphyllus, Ficus auriculata and Calotropis procera. Lat. Americ J Pharm 38, 945-953.

[27] Kigen, G.K., Ronoh, H.K., Kipkore, W.K., Rotich, J.K., (2013). Current trends of traditional herbal medicine practice in Kenya: A review. African J Pharmacol Ther 2, 32-37.

[28] Kigen, G.K., Ronoh, H.K., Kipkore, W.K., Rotich, J.K., (2013). Current trends of traditional herbal medicine practice in Kenya: A review. African J Pharmacol Ther 2, 32-37.

[29] Kipkore, W., Wanjohi, B., Rono, H., Kigen, G., (2014). A study of the medicinal plants used by the Marakwet Community in Kenya. J Ethnobiol Ethnomed 10, Article 24.

[30] Kirtikar, K.R., Basu, B.D., (1995). In: Indian Medicinal Plants, Vols IIV. International Book Distributors, Dehra Dun, India.

[31] Kumar, A. P. N., Kumar, M., Jose, A., Tomer, V., Oz, E., et al., (2023). Major Phytochemicals: Recent Advances in Health Benefits and Extraction Method. Molecules. 28.

[32] Mahajan, M.S., Gulecha, V.S., Khandare, R.A., Upaganlawar, A.B., Gangurde, H.H., Upasani, C.D., (2012). Anti-edematogenic and analgesic activities of Ficus benghalensis. Int J Nutr Pharmacol Neurol Dis 2, 100-104.

[33] Mahajan, M.S., Gulecha, V.S., Khandare, R.A., Upaganlawar, A.B., Gangurde, H.H., Upasani, C.D., (2012). Anti-edematogenic and analgesic activities of Ficus benghalensis. Int J Nutr Pharmacol Neurol Dis 2, 100-104.

[34] Mamedov, N.A., Rzayev, A.A., Shamilov, E.N., Abdullaev, A.S., Rzayeva, I.A., Gasimova, N.I., Guliev, G.N., Craker, L.E., (2011). Radioprotective activity of some medicinal plant extracts. Acta Hortic 925, 315-320.

[35] Marasini, D.R., Pandey, J., Sharma, L.P., Paudel, L., Gyawali, R., Rokaya, R.K., Giri, P.M., Khadka, R.B., Aryal, P., Bhan, R., (2020). Analgesic activity of bark and leaves of Ficus religiosa L. from Nepal. Int J Pharm Pharm Sci 12, 32-35.

[36] Mattson, M.P., (2004). Metal-catalysed disruption of membrane protein and lipid signalling in the pathogenesis of neurodegenerative disorders. Ann N Y Acad Sci 1012, 37-50.

[37] Megersa, M., Tamrat, N., (2022). Medicinal plants used to treat human and livestock ailments in Basona Werana district, North Shewa Zone, Amhara Region, Ethiopia. Evi-Based Complement Alter Med 2022, Article ID 5242033.

[38] Megersa, M., Tamrat, N., (2022). Medicinal plants used to treat human and livestock ailments in Basona Werana district, North Shewa Zone, Amhara Region, Ethiopia. Evi-Based Complement Alter Med 2022, Article ID 5242033.

[39] Mirghazanfari, S.M., Alameh, H.A., Parviz, M., Basir, Z.A., (2019). Evaluation of Ficus carica Linn fruit extracts on formalin induced pain in the male rat paw. Ann Mil Health Sci Res 17, e97383.

[40] Ochatt, S., Alan, A.R., Bhattacharya, A., Hano, C., Kiselev, K.V., Marconi, P.L., et al., (2022). Secondary metabolites: a boon from plants, the best chemist in nature: preface from the editors. Plant Cell Tissue Organ Cult.; 149:1-6.

[41] Pandey, M.M., Rastogi, S., Rawat, A.K., (2013). Indian traditional ayurvedic system of medicine and nutritional supplementation. Evid. Based Complement. Alternat. Med.; 2013:376327.

[42] Pathania, M.S., Sankhyan, P., Sharma, J., Bhardwaj, P., Pathania, S. D., (2021). Antimicrobial activity of Ficus religiosa against some pathogenic microorganisms. Int J Progressive Res Sci Eng 2, 759-763.

[43] Patil, V.V., Patil, V.R., (2011). Evaluation of anti-inflammatory activity of Ficus carica Linn. leaves. Indian J Nat Prod Resour 2, 151-155.

[44] Patil, V.V., Patil, V.R., (2011). Evaluation of anti-inflammatory activity of Ficus carica Linn. leaves. Indian J Nat Prod Resour 2, 151-155.

[45] Penn, G.B., Ashford, A., (1963). The inflammatory response to implantation of cotton pellets in the rat. Journal of Pharmacy and Pharmacology, 15: 798-803.

[46] Piato, A.L., Detanico, B.C., Jesus, J.F., Lhullier, F.L., Nunes, D.S., Elisabetsky, E., (2008). Effects of Marapuama in the chronic mild stress model: Further indication of antidepressant properties. J Ethnopharmacol 118, 300-304.

[47] Qi, C.-C., Fu, Y.-H., Chen, W.-H., Chen, G.-H., Dai, C.-Y., Song, X.-P., Han, C.-R., (2018). A new isoflavone from the roots of Ficus auriculata. Nat Prod Res 32, 43-47.

[48] Rainsford, K. D., Whitehouse, M. W., (1980). Anti-inflammatory/antipyretic salicylic acid esters with low gastric activity. Agents Action. 10:451-5.

[49] Rajdev, K., Jain, S., Mahendra, C.H., Bhattacharaya, S.K., (2018). Ant nociceptive

effects of Ficus bengalensis bark extract in experimental models of pain. Cureus 10, e2259.
[50] Ramakrishna, V., Preeti Gupta, K., Setty, O.H., Kondapia, A.K., (2014). Protective effect of Ficus bengalensis L. extract against H_2O_2 induced DNA damage and repair in neuroblastoma cells. Free Rad Antioxidants 4, 3-7.
[51] Ramakrishna, V., Preeti Gupta, K., Setty, O.H., Kondapia, A.K., (2014). Protective effect of Ficus bengalensis L. extract against H_2O_2 induced DNA damage and repair in neuroblastoma cells. Free Rad Antioxidants 4, 3-7.
[52] Ramprasath, V.R., Shanthi, P., Sachdanandam, P., (2006). Immunomodulatory and anti-inflammatory effects of Semecarpus anacardium Linn nut milk extract in experimental inflammatory conditions. Biological & Pharmaceutical Bulletin, 29 (4): 693-700.
[53] Rao, M.R., Rao, Y.M., Rao, A.V., Prabhaka, M.C., Rao, C.S., Muralidhar, N., Reddy, B.M., (1998). Antinociceptive and anti-inflammatory activity of a flavonoid isolated from Caralluma attenuate. Journal of Ethno pharmacology, 62(1): 63-66.
[54] Santos, F.A., Rao, V.S.N., Silveira, E.R., (1996). Naloxone-resistant anti-nociceptive activity in the essential oil of Psidium pohlianum Berg. Phytomedicine, 3: 197-201.
[55] Serhan, C. N., Savill, J., (2005). Resolution of inflammation: The beginning programs the end. Nat Immunol. 6,1191-7.
[56] Shahinuzzaman, M., Akhtar, P., Amin, N., Ahmed, Y., Anuar, F.H., Misran, H., Akhtaruzzaman, M., (2021). New insights of phenolic compounds from optimized fruit extract of Ficus auriculata. Sci Rep 11, 12503.
[57] Shao, T.-M., Liao, H.-X., Li, X.-B., Chen, G.-Y., Song, X.-P., Han, C.-R., (2022). A new isoflavone from the fruits of Ficus auriculata and its antibacterial activity. Nat Prod Res 36, 1191-1196.
[58] Shao, T.M., Zheng, C.J., Li, X.B., Chen, G.Y., Song, X.P., Han, C.R., (2018). A new12-membered lactone from the stems of Ficus auriculata. Nat Prod Res 32, 2268-2273.
[59] Sharma, B.B., Balakrishnan, N.P., Rao, R.R., Hajra, P.K., (1993). Flora of India. Vol., B.S.I. Calcutta.
[60] Sindhu, R. K., Kumar, P., Singh, I., Arora, S., (2010). Hypoglycemic potential of Verbesina encelioides Benth. roots. Research J. Pharmacognosy and Phytochemistry 2, 41-45
[61] Singh, B., Nathawat, S., Sharma, R.A., (2021). Ethnopharmacological and phytochemical attributes of Indian Tinospora species: A comprehensive review. Arabian J Chem 14, 103381.
[62] Singh, B., Sharma, R.A., (2020). Indian Morinda species: A review. Phytotherapy Res 34, 924-1007.
[63] Swingle, K.F., Shideman, F.E. (1972). Phases of inflammatory response to subcutaneous implantation of cotton pellet and other modifications by certain anti-inflammatory agents. Journal of Pharmacology and Experimental Therapeutics, 183: 226-234.
[64] Tamta, G., Mehra, N., Tandon, S., (2021). Traditional uses, phytochemical, and pharmacological properties of Ficus auriculata: A review. J Drug Deliv Ther 11, 163-169.
[65] Tamuly, C., Buragohain, R., Hazarika, M., Bora, J., Gajurel, P.R., (2015). Assessment of antioxidant activity of six Ficus species-underutilized fruits from Arunachal Pradesh in Northeast India. Int J Fruit Sci 15, 85-99.
[66] Thite, A.T., Patil, R.R., Naik, S.R., (2014). Anti-arthritic activity profile of methanolic extract of Ficus bengalensis: Comparison with some clinically effective drugs. Biomed Aging Pathol 4, 207-217.
[67] Thite, A.T., Patil, R.R., Naik, S.R., (2014). Anti-arthritic activity profile of methanolic extract of Ficus bengalensis: Comparison with some clinically effective drugs. Biomed Aging Pathol 4, 207-217.
[68] Turner, RA., (1965). Screening methods in Pharmacology. Academic Press. New York. 158 p.
[69] Ukwe, CV., (1996). Rheumatoid arthritis. In: Therapeutic Basis of Clinical Pharmacy in the Tropical. SNAAP Press. Enugu, Nigeria.
[70] Veerapur, V.P., Prabhakar, K.R., Parihar, V.K., Kandadi, M.R., Ramakrishana, S., Mishra, B., Satish Rao, B.S., Srinivasan, K.K., Priyadarsini,

K.I., Unnikrishnan, M.K., (2009). Ficus racemosa stem bark extract: A potent antioxidant and a probable natural radio-protector. eCAM 6, 317-324.

[71] Vignesh, M., Priya, V.V., Gayathri, R., (2019). Antistress activity of methanolic extract of Ficus benghalensis. Drug Invent Today 12, 1281-1283.

[72] Vinegar, R., Truax, J.F., Selph, J.L., (1976). Quantitative studies of the pathway to acute Carrageenan inflammation. Federal Proceedings, 35(13):2447-2456.

[73] Vinutha, K., Vidya, S.M., Kumari, S.N., Sanjeev, G., Nagendra, H. G., Pradeepa, Rao, V.C., (2015). Radioprotective activity of Ficus racemosa ethanol extract against electron beam induced dna damage in vitro, in vivo and in silico. Int J Pharm Pharm Sci 7, 110-119.

[74] Winter, C.A., Risley, E.A., Nuss, G.W., (1962). Carrageenan-induced edemas in hind paw of the rat as an assay for anti-inflammatory drugs. Proceedings of the Society for Experimental Biology and Medicine, 111: 545-547.

[75] Zimmermann, M., (1983). Ethical guidelines for investigation of experimental pain in conscious animals. Pain, 109-110.