doi.org/10.36721/PJPS.2022.35.6.REG.1549-1556.1

Anti-inflammatory potential of spectroscopically analyzed trans-13-octadecenoic acid of *Yucca elephantipes* Regel roots: *in-vitro* and *in-vivo* analysis

Muhammad Shoaib Khan[1], Muhammad Uzair[1]*, Muhammad Hanif[2], Mehreen Jabeen[1] and Bashir Ahmad Chaudhary[3]

[1]Department of pharmaceutical chemistry, Faculty of Pharmacy, Bahauddin Zakariya University, Multan, Pakistan
[2]Department of Pharmaceutics, Faculty of Pharmacy, Bahauddin Zakariya University, Multan, Pakistan
[3]Department of Pharmacy, Institute of Southern Punjab, Multan, Pakistan

Abstract: Plants are always better choice for treatment of disease in contrast to synthetic agents due to their less toxicity, and free availability with minor limitations of identifications, purity, and potency which should be addressed. The objective of current study was to explore the anti-inflammatory effect of methanol extract of *Yucca elephantipes* roots by using oxidative burst assay and carrageen an induced rat paw edema. GC-MS analysis was carried for the determination of ani-inflammatory potential of fatty acids and other phytochemicals present in Y*ucca elephantipes* roots. Among fifteen detected compounds *trans*-13-octadecenoic acid, n-hexadecanoic acid and 4-hydroxy benzoic acid were found as 84.21%, 5.21% and 2.17% respectively. Oxidative burst assay showed anti-inflammatory potential of *Yucca elephantipes* roots 74.58±0.32% with IC_{50} of 15.3±2.2µg/mL as compared to Ibuprofen with percentage of inhibition 73.20±0.17% and IC_{50} was 11.2±0.98µg/mL. Fortunately, less than 8g/kg dose of the *Yucca elephantipes* roots found safe in albino rats. Interestingly, *in-vivo* carrageen an induced paw edema method proved its anti-inflammatory potential at dose 100 and 200 mg/kg in albino rats. Conclusively, 200 mg/kg dose of *Yucca elephantipes* roots extract was optimized for 88.89±0.015 % anti-inflammatory effect which can be considered most potent, safe and better alternative of synthetic drugs.

Keywords: Anti-inflammatory potential, carrageenan induced edema, GC-MS analysis, oxidative burst assay and trans-13-octadecenoic acid.

INTRODUCTION

Inflammation is documented as main cause of morbidity around the world (Dewanjee *et al*., 2013). It is a defensive response of an individual towards foreign bodies such as, parasites, viruses and bacteria (Calixto *et al.,* 2003). If inflammation remains untreated, it may cause multiple sclerosis, inflammatory bowel disease, rheumatoid arthritis, immune inflammatory ailment, tumorigenesis and psoriasis (Patil *et al*., 2019). It is well managed by steroidal and non-steroidal drugs in current clinical practice. Up to 70% of people at age of 65 years or more are reported to use NSAIDs 2-3 times per week. But the persistent use of NSAIDs create GI complications, cardiovascular problems and acute kidney disorders (Pountos *et al*., 2011). In addition to these hyperglycemia, hypertension, growth retardation and osteoporosis complications are associated with steroidal anti-inflammatory drugs (Gautam and Jachak, 2009). Reoccurrence of symptoms and toxicity after discontinuation is also another issue related with currently available synthetic anti-inflammatory medicines (Jo *et al*., 2010). There is a challenge for pharmaceutical scientists to identify the natural sources to overcome the draw backs of NSAIDs.

**Corresponding author:* e-mail: muhammaduzair@bzu.edu.pk

To overcome the limitations and side effects of synthetic anti-inflammatory agents (steroidal and NSAID s), the more effective affordable and beneficial alternatives having no or fewer side effects are herbal medicines (Plachetka, 2015; Plachetka, 2016). The acceptance of plant medicines has been increasing due to their impressive, encouraging and biocompatible health outcomes of various clinical trials (Wan *et al*., 2014). It is evident from scientific studies, the natural products from plant sources have been used as folk medicine in treatment of inflammation (Patil, 2019). Phytochemical analysis of plants reveals the presence of several phytoconstituents with anti-inflammatory properties. These phytochemicals are polyphenols, steroids, saponins, fatty acids which exert a synergistic effect in treatment of inflammation (Tripp *et al*., 2012). Most abundant use of fatty acids as an anti-inflammatory agent is described in pervious literature (De-Oliverira *et al*., 2014; Bellik *et al*., 2012).

Genus *Yucca* belongs to family *Agavaceae* which comprises approximately 40 species. This genus is well known in folk medicines. The flowers of *Yucca aloifolia*, roots and bark of *Yucca schidigera*, leaves and roots of *Yucca filamentosa*, leaves of *Yucca schotii* were used traditionally to relief inflammation (Sobia *et al*., 2013; Seema 2012). The extracts of various species of genus

Yucca are used in joint pain and prostate inflammation. (Patel, 2012). *Yucca elephantipes* also known as Giant *Yucca* is growing in Asia (Pakistan) as an ornamental plant. Its flowers have diuretic activity so they are used in kidney disorders (Sotelo *et al*., 2007). Glycoside (furostanol) and steroidal saponin (spirostanol) have been purified successfully from the stem and leaves of *Yucca elephantipes* (Zhang *et al*., 2008; Zhang *et al*., 2013). According to our best of information there are no scientific data presented about use of *Yucca elephantipes* root for the treatment of inflammation.

For the establishment of anti-inflammatory effect of *Yucca elephantipes* roots simple methanolic extract having highest concentrations of fatty acid was used. Therefore, aim of the current study was to identify the phytochemical constituents of *Yucca elephantipes* roots, use of fatty acids as an anti-inflammatory agent *in-vitro* and *in-vivo* analysis. Identified constituents may provide a simple and applicable treatment of inflammation and can be used as an alternative of synthetic drugs.

MATERIAL AND METHOD

Chemicals and reagents

Methanol analytical grade from Merck, DMSO from Sigma Aldrich, Ibuprofen from Pharmagen company, Diclofenac sodium from local supplier.

Plant material

Plant material was collected from Shadaab Nersury, Multan in October 2020, and identified as *Yucca elephantipes* by Prof. Dr. Altaf Dasti, Department of Botany, Bahauddin Zakariya University, Multan, Pakistan. Voucher specimen (Voucher No. YE 1056/DAB/BZU) of collected plant was deposited at herbarium of department of the applied Biology, Bahauddin Zakariya University, Multan. The roots were separated from plant and dried in shade for 65 days.

Preparation of extract

Repeated methanolic extraction of *Yucca elephantipes* roots were performed by slightly modified, already reported method of Handa *et al*., 2008. Briefly; 250g shaded dried roots of *Yucca elephantipes* were ground to powder and soaked in analytical grade methanol for 72h first, at room temperature and then macerated with hydro-methanolic solution for further 72h, successively. Complete removal of the excessive solvent from resulted mixture was done by rotary evaporator under reduced pressure of 40 mmHg. Resulted extract was weighed and stored in airtight container for further use.

Phytochemicals studies

Preliminary phytochemical test

The preliminary phytochemical tests were performed to detect various classes of secondary phytoconstituents in dried powder of *Yucca elephantipes* roots according to standard procedures with some modifications (Banu and Cathrine, 2015). The detection of glycoside, phenols, flavonoids, steroids, triterpenoids and saponins are shown in table 1.

Gas chromatography-Mass spectrometric analysis

GC-MS analysis of biologically active components in methanol extract of *Yucca elephantipes* roots was performed with Agilent Technologies triple quad 7000A (GC model 7890-A) having HP-5 MS column 30m length, 250µm diameter and 0.25µm film thickness. Electron ionization system with high energy electron beam (70 eV) has been used for GC-MS technique. Helium gas with 99.99% purity was used as a carrier gas and flow rate was adjusted to 1mL/min. The started temperature was 50^{o}C that was increased to 200^{o}C at a rate of 5^{o}C/min for 30 min and then increased upto 300^{o}C at the rate of 10^{o}C/ min for 10 min. Temperature of transfer line and injection port was set at 260^{o}C and 250^{o}C, respectively. Dilute sample of methanolic extract of *Yucca elephantipes* roots (1% m/v) of 2.5µL was inserted to split mode (10: 1 ratio). Retention indices of n-alkanes were used in calculating retention indices of components in methanolic extract. HP-5 MS column was used for identification and quantification of compounds in *Yucca elephantipes* roots.

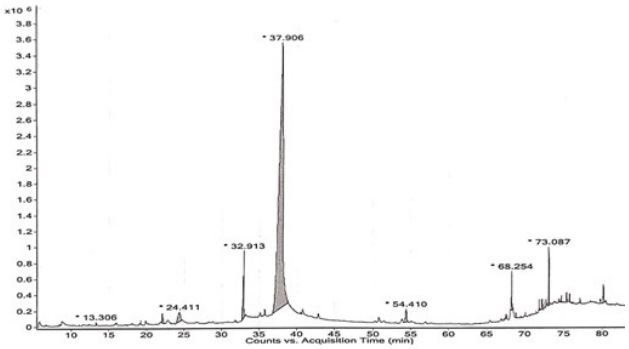

Fig. 1: The GC-MS chromatogram of methanol extract of *Yucca elephantipes* roots.

Oxidative burst assay

Anti-inflammatory potential of methanolic extract of *Yucca elephantipes* roots was determined by means of already reported, slightly modified method of oxidative burst assay (Jabeen *et al*., 2015) Briefly, 10, 20, 30µg /mL solutions of *Yucca elephantipes* roots were prepared in DMSO and incubated with equal ration (1:1) of HBSS^{++} (Hank Balanced Salt Solution having magnesium chloride and the calcium chloride). Test performed in 96 well plates incubated previously in luminometer (thermostate chamber) at 37^{o}C for 2h. The control wells contain only 25uL of HBSS^{++}. Finally add 25µL serum opsonized zymosane and 25µL intracellular reactive species detecting probe (luminol) in each well excluding blank. Level of ROS (reactive oxygen species) was noted via relative light unit in luminometer. The test was performed in triplicate and reported in mean ± SD (n=3).

Table 1: Preliminary phytochemical test of dried roots powder of *Yucca elephantipes*.

Phytochemicals	Tests	Observation	Result
Glycosides	Keller Killiani Test	Reddish brown layer	+
Phenols	$FeCl_3$ Test	Red coloration	+
Steroids	Acetic Anhydride test	Violet to green color	+
Flavonoids	NaOH Test	Yellow coloration	+
Alkaloids	Dragendorff and Wagner Test	No precipitate formation	-
Triterpenoids	Salkowski Test	Reddish brown coloration	+
Saponins	Foam Test	Stable foam formation	+
Anthraquinone	Borntrager test	No color change	-

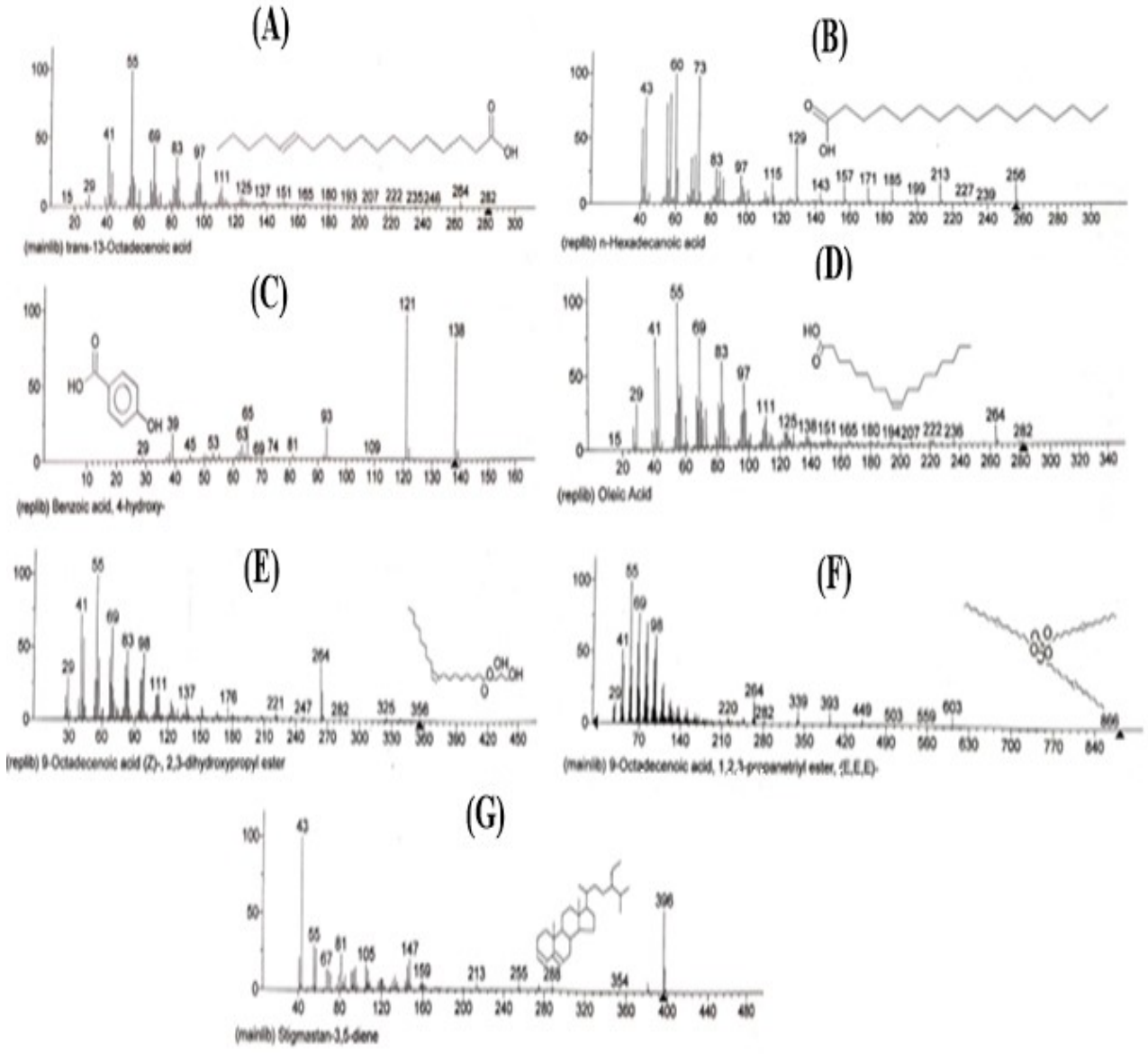

Fig. 2: Mass spectrum of abundant compounds in methanol extract of *Y. elephantipes* roots. (A) Fragmentation pattern of *Trans*-13-Octadecenoic acid; (B) Fragmentation pattern of n-Hexadecanoic acid; (C) Fragmentation pattern of 4-hydroxy benzoic acid; (D) Fragmentation pattern of 9-Octadecenoic acid (Z); (E) Fragmentation pattern of 9-Octadecenoic acid-(Z)-,2,3-dihydroxypropyl ester; (F) Fragmentation pattern of 9-Octadecenoic acid, 1,2,3-propanetriyl ester; (G) Fragmentation pattern of Stigmastan-3,5-diene.

Table 2: Phytochemical profile of methanol extracts of *Yucca elephantipes* roots by GC-MS.

No. of Peaks	Compound Name	Molecular Formula	Class of Compound	Retention Time	Peak Area %
1	3,5-dihydroxy,6-methyl-2,3-dihydro-4(H)-pyran-4-one.	$C_6H_8O_4$	Pyran	13.306	0.12
2	Benzoic acid, 4-hydroxy-, methyl ester	$C_8H_8O_3$	Ester	22.094	0.88
3	4-hydroxy benzoic acid	$C_7H_6O_3$	Phenol	24.411	2.17
4	n-Hexadecanoic acid	$C_{16}H_{32}O_2$	Fatty acid	32.913	5.21
5	*Trans*-13-Octadecenoic acid	$C_{18}H_{34}O_2$	Fatty acid	37.906	84.21
6	9-Octadecenoic acid (Z) (Oleic acid)	$C_{18}H_{34}O_2$	Fatty acid	54.410	1.68
7	9-Octadecenoic acid-(Z),-2,3-dihydroxypropyl ester	$C_{21}H_{40}O_4$	Ester	68.254	1.65
8	1-Heptatriacotanol	$C_{37}H_{76}O$	Alcohol	71.858	0.27
9	Ergost-5-en-3-ol-acetate (3β, 24R)-	$C_{30}H_{50}O_2$	Steroid	72.196	0.30
10	2,5-furandione, dihydro-3-(2-tetradecenyl)-	$C_{18}H_{30}O_3$	Furan	72.282	0.12
11	Stigmasta-5,22-dien-3-ol- acetate (3β)	$C_{31}H_{50}O_2$	Steroid	72.538	0.16
12	Ethyl iso-allocholate	$C_{26}H_{44}O_5$	Steroid	72.766	0.14
13	Stigmastan-3,5-diene	$C_{29}H_{48}$	Steroid	73.087	1.34
14	Stigmast-5-en-3-ol, (3β)-	$C_{29}H_{50}O$	Steroid	75.389	0.33
15	9-Octadecenoic acid-1,2,3-propanetriyl ester (all trans)	$C_{57}H_{104}O_6$	Ester	80.133	1.42

Table 3: Effect of hydro-methanolic extract of *Y. elephantipes* on carrageenan induced rats paw edema.

	Time	Control	Diclofenac sodium	100 mg/Kg	200 mg/Kg
Paw Volume (mL)	0 min	0.048 ± 0.008	0.052 ± 0.008	0.022 ± 0.008	0.056 ± 0.011
	30 min	0.154 ± 0.010	0.092 ± 0.008	0.126 ± 0.009	0.164 ± 0.011
	60 min	0.164 ± 0.011	0.116 ± 0.011	0.136 ± 0.009	0.168 ± 0.013
	120 min	0.154 ± 0.018	0.108 ± 0.013	0.126 ± 0.009	0.120 ± 0.008
	180 min	0.144 ± 0.015	0.094 ± 0.011	0.108 ± 0.008	0.100 ± 0.010
	240 min	0.134 ± 0.015	0.064 ± 0.008	0.100 ± 0.010	0.074 ± 0.011
Percentage Inhibition of paw volume (%)			70.27 ± 0.012	73.56 ± 0.016	88.89 ± 0.015

Table 4: Tukey's test analysis for multiple column comparison of *in-vivo* anti-inflammatory effect of hydro-methanolic extract of *Yucca elephantipes* roots.

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Significant?	Summary	Adjusted P Value
Control vs. Diclofenac sodium	0.046	0.036 to 0.056	Yes	****	<0.0001
Control vs. 100 mg/mL	0.031	0.021to 0.041	Yes	****	<0.0001
Control vs. 200 mg/mL	0.016	0.006 to 0.026	Yes	***	0.0003
Diclofenac sodium vs. 100 mg/mL	-0.015	-0.025 to -0.004	Yes	**	0.0011
Diclofenac sodium vs. 200 mg/mL	-0.030	-0.040 to -0.019	Yes	****	<0.0001
100 mg/mL vs. 200 mg/mL	-0.015	-0.025 to -0.004	Yes	**	0.0011

Oral toxicity studies

Albino red eyes mice were treated with hydro-methanol extract of *Yucca elephantipes* roots with different concentrations from 200mg/Kg to 8000 mg/kg. The mice were kept under observation for 14 days and mortality was observed and recorded twice daily (Jantawong *et al.,* 2021).

Carrageenan induced rat paw edema

For investigation of *in-vivo* anti-inflammatory potential, the most commonly method is inhibition of edema formed in rat's hind paw. The effect is measured by computerized plethysmometer method. The Wister albino rats of 100-150g (male or female) were used for inducing oedema in left paw by injecting 0.1mL carrageenan solution in physiological saline. The hydro-methanol extract at concentrations 100 mg/kg and 200mg/kg was orally administered 30 min before injecting carrageenan. Paw volume was measured by plethysmograph (mercury displacement method) at interval of 30, 60, 120, 180 and 240 minutes. The percent inhibition of each concentration of extract was compared diclofenac sodium (standard drug) at concentration of 5 mg/kg (Hanif *et al*., 2021).

Ethical approval

This study has been reviewed and approved by animal ethics committee of Bahauddin Zakariya University, Multan. White albino mice were used and maintained under clean condition at 23±2^{o}C with humidity 40-60% and fed commercially available diet.

STATISTICAL ANALYSIS

Results are stated as mean ± SD (standard deviation) by using single factor ANOVA for multiple comparisons. P values (<0.05) were found to be statistically significant. A post hoc statistical analysis Tukey's test was performed for the comparisons between control and standard, control and 100mg/kg and 200mg/kg hydro-methanolic extract of *Yucca elephantipes* roots, standard and 100mg/kg and 200mg/kg hydro-methanolic extract of *Yucca elephantipes* roots, and 100mg/kg was compared with 200mg/kg hydro-methanolic extract of *Yucca elephantipes* roots respectively.

RESULTS

Total fifteen components of steroids, fatty acids, phenols, esters, alcohols, pyrans, and furans classes were detected in the methanolic extract of *Yucca elephantipes* roots by GC-MS technique and are given in table 2. The GC-MS chromatogram is showed in fig. 1 and mass spectrum of abundant components are shown in fig. 2. The methanol extract of *Yucca elephantipes* root exhibited remarkable anti-inflammatory activity with IC_{50} value 15.3±2.2µg/mL as compared to standard 11.2±1.9µg/mL. The methanol extract of *Yucca elephantipes* roots exhibit maximum ROS inhibition 76.646% at concentration of 30µg/mL as compared to standard ibuprofen (73.203%). The results are explained in fig. 3.

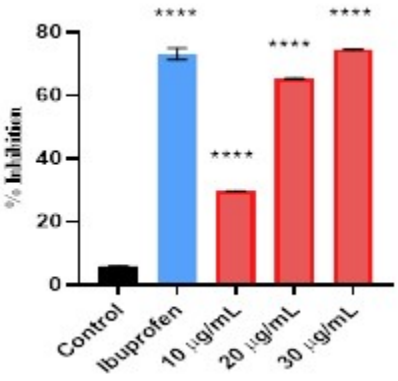

Fig. 3: *In-vitro* anti-inflammatory potential of methanol extract of *Yucca elephantipes* roots. P<0.0001.

The oral toxicity studies were performed to evaluate the mortality rate of animals. The mice fed with maximum 8000mg/kg dose was found to be dead after 48h of observation. The administration of 1% carrageenan solution in sub-plantar area of rat's left paw causes edema. The anti-inflammatory potential was evaluated by carefully monitoring the volume changes in edema. Administration of carrageenan saline solution causes significant rise in thickness of rat's paw after 1, 2, 3 and 4h. Hydro-methanolic extract of *Yucca elephantipes* roots at concentrations 100mg and 200 mg started to reduce edema after 120min. The hydro-methanolic extract of *Yucca elephantipes* roots, showed the maximum 88.89± 0.015% inhibition of edema at 200mg/kg dose as compared to standard diclofenac sodium, which showed 70.27± 0.012% at 5mg/kg. The percentage inhibition and anti-inflammatory effect at different time interval and doses are given in table 3. The comparison of extract and standard with control is shown in fig. 4. The result was analyzed by Tukey's test for multiple comparison of column. The comparison of control with standard and hydro-methanolic extract of *Yucca elephantipes* roots (100 and 200 mg/kg) are given in table 4.

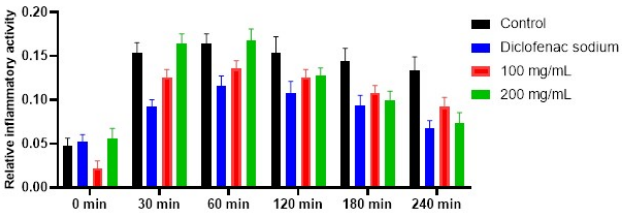

Fig. 4: Anti-inflammatory potential of hydro-methanol extract of *Y. elephantipes* roots on carrageenan-induced rat's paw edema. P<0.0001.

DISCUSSION

In present study, phytochemicals of methanol extract of *Yucca elephantipes* roots were evaluated by the GC-MS analysis, and fatty acid is found to be most abundant class with respect to percentage area. *Trans*-13-octadecenoic acid (unsaturated fatty acid) is present in highest concentration (84.21%) detected by the strong peak in GC-MS chromatogram. Hameed *et al*., (2016) reported enhanced anti-inflammatory activity of unsaturated fatty acids by producing the pro-resolving lipid mediators from EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid). EPA metabolized into resolvins and DHA metabolized into protectin, maresins and resolvins. The biological effect of resolvins, protectins and maresins have been described in reducing the inflammation on the basis of cell culture and animal models. These compounds reduce the inflammation by inhibiting the infiltration of neutrophils at inflamed site, by inhibition of IL-Iβ synthesis (pro-inflammatory cytokins) and Tumor necrosis factor-alpha (Calder, 2017). n-hexadecanoic acid (palmitic acid) was found as second most abundant constituent with percentage area 5.21% and also found effective against inflammation and rheumatism (Aparna *et al*., 2012; Uchegbu *et al*., 2015). Karagoz *et al*., 2015) reported that 9-Octadecenoic acid (Z)- is effective against atherosclerosis. It is found in concentration 1.6% in methanolic extract of *Yucca elephantipes* roots. n-hexadecanoic acid and 9-octadecenoic acid exert synergistic anti-inflammatory effect with *trans*-13-octdecenoic acid, which makes *Yucca elephantipes* roots more effective in reducing inflammation.

Third major compound in roots extract was 4-hydroxybenzoic acid (Paraben) with percent area 2.17%. Manuja *et al*. (2013) has been reported its anti-

inflammatory potential. Srivastava *et al*., (2015) also reported anti-inflammatory and antispasmodic effects of 9-octadecenoic acid, 1, 2, 3-propanetriyl ester (E, E, E), which is present in 1.42%. Stigmastan-3, 5-diene is a steroid, which has 1.34% area. Altememe *et al.,* (2015) recognized this compound as anti-inflammatory and antiulcer agent. Stigmast-5-en-3-ol, (3β)- (0.33% area) is another steroid with anti-inflammatory activity (Ambavade *et al*., 2014). 1-heptatriacotanol (0.27%) is alcohol which possess anti-inflammatory, anticancer and antioxidant potentials (Al-Rubaye *et al*., 2017). Ethyl allocholate (0.14%) have different pharmacological effect including, anti-inflammatory, relieving arthritis and asthma (Vijayabaskar and Elango, 2018). In addition to these, 3,5-dihydroxy-6-methyl-2,3-dihydro-4H-pyran-4-one (0.12%) exhibit anti-inflammatory, antitumor and antioxidant activities (Mopuri *et al*., 2018; Uchegbu *et al*., 2017).

The high contents of fatty acid revealed that the methanolic extract of *Yucca elephantipes* roots should have strong anti-inflammatory potential, therefore the *in-vitro* and *in-vivo* anti-inflammatory studies were conducted. *In-vitro* anti-inflammatory potential was determined by oxidative burst assay, in which level of reactive oxygen species (ROS) was recorded. According to Feniouk and Skulachev (2017), ROS are basically free radicals including hydroxyl radicals, hydroperoxyl radicals, super oxide anion, nitric oxide and singlet of oxygen derive from molecular oxygen.

These species are generated from mitochondria through electron transport chain. These ROS has ability to damage the biomolecules on the other hand, they also involve in the regulation of cell growth, cell adhesion cell differentiation and cell death (Kalinina *et al*., 2014). Various evidences describe the role ROS in resolution of inflammation. Chelombitko (2018) declared that ROS resolve inflammation by multiple events. Lopes *et al*., (2011) have proved that ROS resolve inflammation by the apoptosis of neutrophils. Another anti-inflammatory event is destabilization of NADPH oxidase mRNA by RNA binding proteins, which leads to decrease in ROS production and activates macrophages. These macrophages induce phagocytosis of apoptotic cell, which leads to decrease inflammation (Kuchler *et al*., 2014). Tan *et al*., (2016) enlightened that ROS are involved in expression of proinflammatory cytokines by maintaining the proinflammatory phenotype of macrophages. The level of ROS should to reduce to treat the inflammation. The results revealed that the IC_{50} value of methanol extract of *Yucca elephantipes* roots is 15.3±2.2µg/mL which is very closed to ibuprofen (11.2±1.9µg/mL). The promising results of *in-vitro* anti-inflammatory activity revealed that methanolic extract of *Yucca elephantipes* roots have strong potential to decrease ROS level for reducing the inflammation.

The safety of drug and plant extract is evaluated by animal models. The oral toxicity was evaluated by administration of more than five concentrations of hydro-methanol extract of *Yucca elephantipes* roots ranges 200 to 8000mg/kg. The mortality of mice was observed at concentration 8000mg/kg, which was considered as oral toxic dose. Carrageenan induces paw edema is used for evaluation of anti-inflammatory effect of plant extracts and their constituents. Carrageenan is a polysaccharide, which induces paw edema in two stages. The first stage is induced by the bradykinin, histamine and serotonin release, in 0-1h. while, the second stage starts after 3h of carrageenan injection and is mediated by the release of prostaglandin and several other cytokines including, IL-β, TNF-α, IL-6 and IL-10 (Attah *et al*., 2022). In present study we explore that *Yucca elephantipes* roots causes inhibition of edema in dose dependent pattern. The hydro-methanolic extract showed 88.89±0.015% inhibition of inflammation significantly after 240 min at 200 mg/kg without any side effect and mortality, while 73.56±0.016% inhibition at 100mg/kg, as compared to standard 70.27±0.012% significantly after 240 min. Both extract (100mg/kg and 200mg/kg) and standard significantly decreases the inflammation as compared to control. The result is appealing that the extract of *Yucca elephantipes* roots has more potential to inhibit the inflammation due to presence of wide range of phytochemicals as compared to single active pharmaceutical ingredient in synthetic drugs.

CONCLUSION

From the results of present studies, it has been concluded that the roots of *Yucca elephantipes* are the wide and reliable source of potent anti-inflammatory compounds. On the account of *in-vitro* and *in-vivo* anti-inflammatory activities, the roots of *Yucca elephantipes* has been found the safest alternative of synthetic drugs. For future prospect, activity guided isolation and human studies should be performed to discover potent novel anti-inflammatory compounds and to resolve the problems and challenges of inflammation and its associated disorders. This effort will open the new era for scientist and industrialist to isolate the new anti-inflammatory compounds from roots of *Yucca elephantipes* with no or low side effects. The herbalist may recommend these roots to treat inflammation without toxicity.

REFERENCES

Al-Rubaye AF, Kaizal AF and Hameed HI (2017). Phytochemical screening of methanolic leaf extract of *Malva sylvestris*. *Int. J. Pharmacogn. Phytochem*. *Res.,* **9**(4): 537-552.

Altameme HJ, Hameed IH and Abu-Serag NA (2015). Analysis of bioactive phytochemical compounds of two medicinal plant *Equisetum arvense* and *Alchemila valgaris* seeds using gas chromatography-mass

spectroscopy and fourier-transform infrared spectroscopy. *Malays. Appl. Biol*., **44**(4): 47-58.

Ambavade SD, Misar AV and Ambavade P (2014). Pharmacological, nutritional and analytical aspects of β-sitosterol: A review. *Ori. Phar. Exp. Med.,* **14**(3): 193-211.

Aparna V, Kalarickal V, Pradeep KM, Karthe P, Sadasivan C and Haridas M (2012). Anti-inflammatory property of n-hexadecanoic acid: Structural evidence and kinetic assessment. *Chem. Biol. D. Des.,* **80**(3): 434-439.

Attah EI, Ugwuagbo SC, Chinnam S, Eze FI, Nnadi CO, Agbo MO, Obonga W, Rudrapal M, Walode SG, Nizam A, Sahoo RK, Bendale AR, Khairnar SJ and Jagtap MR (2022). Anti-inflammatory activity of *Sabicea brevipes* Wernharm (*Rubiaceae*). *Pharmacia*, **69**(2): 311-317.

Banu KS and Cathrine L (2015). General techniques involved in phytochemical analysis. *Int. J. Adv. Res. Chem*. *Sci.,* **2**(4): 25-32.

Bellik Y, Boukra L, Alzahrani HA, Bakhotmah BA, Abdellah F, Hammoudi SM and Iguer-Ouada M (2012). Molecular mechanism underlying anti-inflammatory and antiallergic activities of phytochemicals: An update. *Mol*., **18**(1): 322-353.

Calder PC (2017). Omega-3 fatty acids and inflammatory processes: From molecules to man. *Biochem. Soc. Trans*., pp.1-11.

Calixto JB, Otuki MF and Santos ARS (2003). Anti-inflammatory compounds of plant origin. Part I action on arachidonic acid pathway, nitric oxide and nuclear factor kB (NF-kB). *Plant Med*., **69**(11): 973-983.

Chelombitko MA (2018). Role of reactive oxygen species in inflammation: A minireview. Moscow University biological sciences bulletin. **73**(4): 242-246.

De-Oliveira RG, Mahon CAPN, Ascencio, PGM, Ascencio SD, Balogun, SO and Martins, DTDO (2014). Evaluation of anti-inflammatory activity of hydroethanolic extract of *Dilodendron bipinnatum* Radlk. *J. Ethanopharmacol*., **155**(1): 387-395.

Dewnajee S, Dua IK and Sahu R (2013). Potential anti-inflammatory effect of *Leea macrophylla* Roxb. leaves: A wild edible plant. *Food Chem. Toxi*., **59**(1): 514-520.

Dzoyem JP, Mcgaw LJ, Kuete V and Bakowsky (2017). Anti-inflammatory and anti-nociceptive activities of African medicinal species and vegetables. *Med. Spi. Veg. Africa*, Chapter 9, pp.239-270.

Feniouk BA and Skulachev (2017). Cellular and molecular mechanism of action of mitochondria-targeted antioxidants. *Curr. Aginh Sci*., **10**(1): 41-48.

Gautum R and Jachak SM (2009). Recent developments in anti-inflammatory natural products. *Med. Res. Rev*., **29**(5): 767-820.

Hameed IH, Altameme HJ and Mohammed GJ (2016), Evaluation of antifungal and antibacterial activity and analysis of bioactive phytochemical compounds of *Cinnamomum zeylanicum* (Cinnamon bark) using gas chromatography-mass spectrometry. *Ori. J. Chem.,* **32**(4): 1769-1788.

Handa SS, Khanuja SPS, Longo G and Rakesh DD (2008). Extraction technologies of medicinal and aromatic plants, no. 66 Italy. United nation industrial development organization and the international centre for science and high technology. pp.1-266

Hanif M, Ameer N, Mahmood MK, Shehzad A, Azeem M, Rana HF and Usman M (2022). Improved anti-inflammatory effect of curcumin by designing self-emulsifying drug delivery system. *Develop. Ind. Phar*., **47**(9): 1-8.

Jabeen M, Arshad F, Uzair M, Chaudhary BA, Jillani U and Zafar Z (2015). Phytochemical screening and biological potential of Phylo nodiflora (Verbenaceae) and Pterospermium acerifolium (Sterculiaceae). *J. Pharm. Bio.,* **5**(3): 230-234.

Jantawong C, Priprem A, Intuyod K, Pairojkul C, Pinlaor P, Waraasawapati S, Mongkon I, Chamgramol Y and Pinlaor S (2021). Curcumin-loaded nanocomplexes: Acute and chronic toxicity studies in mice ans hamsters. *Toxi. Report*. **8**: 1346-1357.

Jo WS, Yang KM, Choi YJ, Jeong CH, Ahn KJ, Nam BH, Lee SW, Seo SY and Jeong MH (2010). *In-vitro* and *in-vivo* anti-inflammatory effects of pegmatite. *Mol. Cell. Toxicol*., **6**: 195-202.

Kalinina EV, Chernov NN and Novichkova MD (2014). Role of glutathione transferase and glutaredoxin in regulation of redox-dependent processes. *Biochem*., **79**(13): 1562-1583.

Krishnamoorthy K and Subramaniam P (2014). Phytocheimcal profiling of leaf, stem and tuber parts of *Solena amplexicaulis* (Lam.) Gandhi using GC-MS. *Int. Sch. Res. Not*., 2014: Article ID 567409, 1-13

Kuchler L, Giegerich AK, Sha LK, Knape T, Wong MS, Schroder K, Branes RP, Heide H, Wittig I, Brune B and von Knethen A (2014). SYNCRIP-dependent Nox2 mRNA destabilization impairs ROS formation in M2-polarized macrophages. *Antioxi.. Redox Sig.* **21**(18): 2483-2497.

Lopes F, Coelho FM, Costa VV, Vieira EL, Sousa LP, Silva TA, Vieira LQ, Teixeira MM and Pinho V (2011). Resolution of neutrophilic inflammation by H2O2 in antigen-induced arthritis. *Arthri. Rheum.,* **63**(9): 2651-2660.

Manuja R, Sachdeva S, Jain A and Chaudhary J (2013). A comprehensive review on biological activities of p-hydroxy benzoic acid and its derivative. *Int. J. Pharm. Sci. Rev. Res.,* **22**(2): 109-115.

Mopuri R, Ganjayi M, Meriga B, Koorbanally NA and Islam MS (2018). The effect of *Ficus carica* on the activity of enzymes related to metabolic syndrome. *J. Food and Drug Ana.,* **26**(1): 201-210.

Patil KR, Mahajan UB, Unger BS, Goyal SN, Bekemkar S, Surana SJ, Ojha S and Patil CR (2019). Animal models of inflammation for screening of anti-inflammatory drugs: Implications for the discovery and

development of phytopharmaceuticals. *Mol. Sci.,* **20**(1): 1-38.

Plachetka JR (2015). Pharmaceutical composition for coordinated delivery of NASIDs. US9161920.

Pountos I, Georgpul T, Bird H and Giannoudis PV (2011). Nonsteroidal anti-inflammatory drugs: Prostaglandins, indications and side effects. *Int. J. Interf. Cytok. Medi. Res*., **3**: 19-27.

Seema P (2012). *Yucca*: a medicinally significant genus with manifolds therapeutic attributes. *Nat Prod Biopros.,* **2**(6): 231-234.

Sotelo A, Lopez-Gracia S and Basurto-Pena F (2007). Contents of nutrients and antinutrient in edible flower of wild plants in Maxico. *Plant Food Hum. Nut.,* **62**(3): 133-138.

Srivastava R, Mukerjee A and Verma A (2015). GC-MS analysis of phytocomponents in, pet. ether fraction of *Wrightia tinctoria* seed. *Pharmacog. J.,* **7**(4): 249-253.

Tan HY, wang N, Li S, Hong M, Wang X and Feng Y (2016). The reactive oxygen species in macrophages polarization: Reflecting its dual role in progression and treatment of human diseases. *Oxid. Med. Cell. Longev*., 2795090.

Tripp ML, Babish JG, Bland JS, Hall AJ, Konda V and Pacioretty LM (2012). Anti-inflammatory botanical products for treatment of rome and diabetes. US8206753.

Uchegbu RI, Bako SS, Ngozi-Olehi LC and Achinihu LO (2015). GC/MS analysis and identification of phytochemicals present in the fruits of *Mormodica balsamina* Linn. *J. Appl. Chem.,* **8**(8): 39-42.

Vijayabaskar G and Elango V (2018). Determination of phytocompounds in *Withania somnifera* and Smilax china using GC-MS technique. *J. Pharmacogn. Phytochem.,* **7**(6): 554-557.

Wan P, Chen H, Guo Y and Bai A (2014). Advances in treatment of ulcerative colitis with herbs: From bench of beside. *World J. Gastroent.,* **20**: 14099-14104.

Zhang Y, Zhang YL, Jacob MR, Li XL and Yang CR (2008). Steroidal saponins from the stem of *Yucca elephantipes*. *Phytochem.,* **69**(1): 264-270.

Zhang Y, Yang CR and Zhang YJ (2013). New steroidal saponins from the leaf of *Yucca elephantipes*. *Helvetica Chimica. Acta,* **96**(9): 1807-1813.