

## Analgesic and anti-inflammatory activity of $\beta$ -sitosterol isolated from leaves of *Oxalis corniculata*

Santosh B Dighe<sup>1\*</sup>, Bhanudas S Kuchekar<sup>2</sup> and Sagar B Wankhede<sup>3</sup>

<sup>1</sup>Department of Pharmacology, Pravara Rural College of Pharmacy, Pravaranagar, Maharashtra, (India)

<sup>2</sup>Department of Pharmaceutical Chemistry, MAEER's, Maharashtra Institute of Pharmacy, Pune Maharashtra, (India)

<sup>3</sup>Department of Pharmaceutical Chemistry, Padmashri Dr. D. Y. Patil Institute of Pharmaceutical Sciences and Research, Pune, Maharashtra, (India)

### Corresponding author\*

Mr. Santosh B. Dighe

Head, Department of Pharmacology,

Pravara Rural College of Pharmacy,

Pravaranagar, Maharashtra, (India), PIN- 413736

Mob. No. 09960465068, Fax No. 02422-273528

E-mail: [sbdigheprcop@gmail.com](mailto:sbdigheprcop@gmail.com)

### Abstract

*Oxalis corniculata* Linn. (Oxalidaceae) is one of the important medicinal plants used traditionally for the treatment of fever, pain and inflammation. To validate folk use of *Oxalis corniculata* as analgesic and anti-inflammatory remedy. The leaves of *Oxalis corniculata* was used for successive extraction with increasing polarity solvents. Petroleum ether extract was selected for activity guided fractionation to isolate  $\beta$ -sitosterol due to its better efficacy than other extracts. Analgesic activity was done by hot plate test and acetic acid-induced writhings, while anti-inflammatory activity by carrageenan-induced paw edema method. All the extracts were screened at the dose of 100 mg/kg, i.p. and isolated  $\beta$ -sitosterol was screened at the doses of 5, 10 and 20 mg/kg, i.p. Naloxone (1 mg/kg, s.c.) was used to understand the mechanism of nociception. In hot plate test, Petroleum ether extract was found most active with reaction time of  $8.4 \pm 0.4$  sec after 60 min while isolated  $\beta$ -sitosterol at dose of 20 mg/kg showed  $11.1 \pm 0.3$  sec after 90 min. The number of writhings in 30 min was compared with paracetamol. Petroleum ether extract and  $\beta$ -sitosterol (20 mg/kg) showed  $43.14 \pm 1.9$  and  $34.21 \pm 1.4$  writhings respectively. Isolated  $\beta$ -sitosterol (20 mg/kg) inhibited rat paw edema to  $0.32 \pm 0.06$  ml after 120 min. Naloxone reversed antinociceptive effects of extracts and isolated  $\beta$ -sitosterol. It can be concluded that isolated  $\beta$ -sitosterol is responsible for analgesic and anti-inflammatory activity of *Oxalis corniculata* leaves and it works through central mechanism.

**Keywords:** *Oxalis corniculata* Linn, Analgesic, Anti-inflammatory,  $\beta$ -sitosterol.

### 1. Introduction

Many plants conveniently available in India are used in traditional folklore medicine for the treatment of fever, pain and inflammation. The plant selected for present studies is *Oxalis corniculata* (Oxalidaceae), very common weed found throughout warmer parts of India. [1] The whole plant traditionally used for anti-inflammatory and antidysentric properties [2] Soup of Indian sorrel is used in diarrhea. [3,4] Its anti-inflammatory [5] and wound healing [6] property has been reported in 1977 and 2004. Also it has antimicrobial [7] and a smooth muscle relaxant property. [8] It was also reported that plant has hypoglycemic, antipsychotic, nervous system stimulant and have chronotropic and inotropic effect. Chemical characterization showed the presence of niacin, vitamin C,  $\beta$ -carotene, glyoxylic acid, oxalic acid, pyruvic acid, vitexin and isovitexin, vitexin-2-O-beta-D-glucopyranoside, neutral lipids, glycolipids, phospholipids, fatty acids, saturated (C10-C14) acids, alpha and beta tocopherols. [9] Phytochemical investigations of *Oxalis corniculata* have revealed the presence of tannins, palmitic acid, a mixture of 8 oleic, linoleic, linolenic and stearic acids. Methanolic and ethanolic extracts of this plant show the presence of carbohydrate, glycosides, phytosterols, phenolic compounds, flavonoids, proteins (12.5%), amino acids and volatile oil. It also showed the presence of calcium, fiber and tannin. Leaves contain tartaric acid and citric acids, calcium oxalate, flavones (acacetin and 7,4'- diOMe apigenin), glycoflavones (4'-OMe vitexin, 4'- OMeiso-vitexin and 3',4'-diOMe orientin), flavonols (3',4'-diOMe quercetin) and phenolic acids such as p-hydroxybenzoic, vanillic and syringic acids. This herb is well known to have an acid taste due to the high content of oxalate in its leaves and stems.[10]

Present study was designed to evaluate analgesic and anti-inflammatory potential of various leaf extract of *Oxalis corniculata*.

## 2. Materials and methods

### 2.1 Plant material

Leaves of *Oxalis corniculata* were collected in the month of January 2014 from Loni (Shirdi) in the Ahmednagar district of Maharashtra. It was authenticated by Dr. Diwakar, Joint Director of Botanical Survey of India, Pune. A voucher specimen (DSOC001) has been deposited in the herbarium section of the department of Pharmacognosy, PRCOP, Loni, for future reference. The leaves (1.5 kg) were air dried and pulverized using a mechanical grinder.

### 2.2 Extraction and isolation

Dried and powdered leaves (250 g) of the plant were extracted successively with various solvents viz. petroleum ether, chloroform, ethyl acetate and methanol in Soxhlet extractor. Extracts were concentrated by vacuum distillation and then dried in open air to produce the respective extracts. All the extracts were vacuum dried to obtain petroleum ether extract (7.24%), chloroform extract (6.034%), ethyl acetate extract (4.48%) and methanol extract (8.54%), respectively.

The petroleum ether extract (5.0 g) was subjected to column chromatography on silica gel column. The column was eluted by gradient elution method using hexane and ethyl acetate with increasing polarity. Fractions of 97-105 eluted with 3% ethyl acetate in hexane were found similar on TLC with a major spot and a minor spot. The concentrated solution was kept for 24 h at room temperature to precipitate needle-shaped crystals. The resultant crystals were separated from liquid phase and washed successively with pure hexane and 1, 2 and 5% ethyl acetate in hexane. The white substance (30 mg) was re-crystallized from methanol and it showed a single spot on TLC (Rf 0.47, ethyl acetate-hexane, 2:8). The isolated compound was identified by studying its melting point, UV, FTIR, MS, <sup>1</sup>HNMR and <sup>13</sup>CNMR spectroscopy.

### 2.3 Animals

Male albino mice (Swiss strain) weighing 25-30 g were housed under standard laboratory conditions, in groups of six each and used for analgesic activity. Wistar Albino rats (150-200 g) were used for screening of anti-inflammatory activity. The animal had free access to water and food *ad libitum*. The ethical committee of the institute approved the protocol of the study having IAEC no. 448/01/c/CPCSEA/13-14/17

### 2.4 Drugs and chemicals

The following drugs and chemicals were used. Drugs: pentazocine lactate injection (Ranbaxy, India), paracetamol injection (Heilenlab, India) and naloxone hydrochloride injection (Reliance Life science, India) purchased from a commercial source. Chemicals: petroleum ether (60-80°C) AR, chloroform AR, ethanol AR, ethyl acetate AR and Tween 80 AR (PCL, India).

### 2.5 Analgesic activity by hot plate test

Central nociceptive activity was evaluated using the hot plate method. [11] Male albino mice (Swiss strain) were divided into 11 groups of six animals each. The first group served as control and received only vehicle (10% Tween 80 in distilled water) and the second group was administered standard drug pentazocine (10 mg/kg, i.p.). The animals of third to seventh groups were treated with extract of petroleum ether (PEOC), chloroform (CFOC), ethyl acetate (EAOC) and methanol (MEOC) of *Oxalis corniculata* leaves (100 mg/kg, i.p., each), respectively. The animals of seven to nine were treated with isolated  $\beta$ -sitosterol (5, 10 and 20 mg/kg, i.p.), respectively. The animals of the 10<sup>th</sup> and 11<sup>th</sup> groups were treated with pentazocine (10 mg/kg, i.p.) and isolated  $\beta$ -sitosterol (10 mg/kg, i.p.) 15 min after naloxone (1 mg/kg, s.c.) administration, respectively. All the extracts, standard drug and isolated  $\beta$ -sitosterol were dissolved into the vehicle. The mice were placed individually on the hot plate maintained at  $55 \pm 0.2^\circ\text{C}$  and latency of nociceptive response such as licking, flicking of the hind limbs or jumping was noted. The readings were taken at 0, 30, 60, 90, 120 and 150 min after treatment. The experiment was terminated 20 s after their placement on the hot plate to avoid damage to the paws.[12]

### 2.6 Analgesic activity by acetic acid-induced writhing test

Peripheral nociceptive activity was evaluated using acetic acid-induced writhing test. [13] Mice were divided into nine groups of six animals each. The first group served as control, which was treated with vehicle only (10% Tween 80 in distilled water). The second group was administered standard drug paracetamol (50 mg/kg, i.p.). The animals of the third to nine groups were treated with petroleum ether (PEOC), chloroform (CFOC), ethyl acetate (EAOC) and methanol (MEOC) extracts of *Oxalis corniculata* leaves (100 mg/kg, i.p., each) and isolated  $\beta$ -sitosterol (5, 10 and 20 mg/kg, i.p.) respectively, 30 min prior intra-peritoneal injection of 0.6% solution of acetic acid (10 ml/kg). All the extracts, standard drug and isolated  $\beta$ -sitosterol were dissolved in the vehicle. After acetic acid injection, the mice were observed for the number of writhing responses for the period of 30 min for each animal. [14]

### 2.7 Anti-inflammatory activity by carrageenan-induced hind paw edema method

Anti-inflammatory activity was evaluated using carrageenan-induced hind paw edema method. Wistar rats of either sex were divided into nine groups of six animals each. The first group received only vehicle (10% Tween 80 in distilled water) served as control and the second group was administered standard drug ibuprofen (50 mg/kg, i.p.). The animals of the third to ninth groups were treated with petroleum ether (PEOC), chloroform (CFOC), ethyl acetate (EAOC)

and methanol (MEOC) extracts of *Oxalis corniculata* leaves (100 mg/kg, i.p., each) and isolated  $\beta$ -sitosterol (5, 10 and 20 mg/kg, i.p.), respectively. All the extracts, standard drug and isolated  $\beta$ -sitosterol were dissolved in the vehicle. After 30 min of the above treatments, 0.05 ml of 1% w/v carrageenan in saline was injected into the subplantar tissue of the left hind paw of the animals. The degree of paw edema of all the groups was measured using plethysmometer at 0, 30, 60, 90 and 120 min after the administration of carrageenan to each group; 0 min readings are the initial paw volume of animals. [15]

### 2.8 Statistical analysis

All data were expressed as mean  $\pm$  SEM. The statistical analysis of all the observations was carried out using one-way ANOVA followed by multiple comparison test of Tukey-Kramer, where necessary.  $P < 0.05$  was considered as significant compared with the control group.

## 3. Results

### 3.1 Identification of isolated compound

The isolated compound was a crystalline solid which is having melting point at 136-138°C and single spot on TLC with  $R_f$  0.47 (ethyl acetate/hexane, 2:8). The isolated compound gave positive Libermann–Burchard test which shows that the compound was a sterol. The mass spectrum showed M at  $m/z$  at 414, corresponding to the molecular formula ( $C_{29}H_{50}O$ ). The IR spectrum showed the occurrence of O-H stretching at ( $3450\text{cm}^{-1}$ ), C-H stretching at ( $2930\text{cm}^{-1}$ ), C=C stretching at ( $1625\text{cm}^{-1}$ ), C-O stretching at ( $1163$  and  $1150\text{cm}^{-1}$ ) and C-H bending at ( $1445$ ,  $1405$ ,  $1375$  and  $1320\text{cm}^{-1}$ ), respectively. The result shows two singlets at  $\delta$  1.00 and 0.67 that were assigned to the methyl group of C-19 and C-18, respectively, in  $^1\text{H-NMR}$  spectrum. The doublets at  $\delta$  0.92 (d,  $J = 6.1\text{ Hz}$ ), 0.81 (d,  $J = 6.9\text{ Hz}$ ), 0.83 (d,  $J = 6.9\text{ Hz}$ ) and 0.84 (t,  $J = 7.3\text{ Hz}$ ) accounted for the methyl group at C-21, C-26 and C-27. Signals at  $\delta$  5.35 in  $^1\text{H-NMR}$  can account for an olefinic proton at C-6. Other multiplet at  $\delta$  3.52 equivalent to a singlet proton was assigned for the proton of C-3. The low field signal may be due to the attachment of b-OH group at the C-3 carbon. Thus, the assignment of hydroxyl group at C-3 and the double bond at C-5 were assigned accordingly. Three multiplets equivalent to two protons each appeared at  $\delta$  1.83, 2.00 and 2.27 and were assigned to three  $\text{CH}_2$  groups. The remaining protons appeared as multiplets at  $\delta$  1.05-1.65. From all the spectral analysis and Co-TLC with authentic sample, the isolated compound was identified as  $\beta$ -sitosterol.  $^{13}\text{C-NMR}$  gave signal at 140.8 and 121.7 ppm for  $\text{C}_5=\text{C}_6$  double bond, respectively, 71.8 for C3 b-hydroxyl group, and 19.4 and 11.9 for the angular methyl carbon atoms for  $\text{C}_{19}$  and  $\text{C}_{18}$ , respectively. (Figure 1)

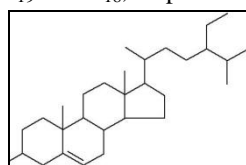


Figure 1: Structure of  $\beta$ -sitosterol

### 3.2 Hot plate test

In the hot plate test, petroleum ether extract (100 mg/kg, i.p.) showed significant increase in reaction time as compared to control and other extracts. Hence, it was subjected to activity-guided fractionation to give  $\beta$ -sitosterol. Isolated  $\beta$ -sitosterol (5, 10 and 20 mg/kg, i.p.) showed promising dose-dependent activity comparable to the standard drug pentazocine (Table 1). To study the involvement of opioid receptors, isolated  $\beta$ -sitosterol was given after opioid antagonist, naloxone (1 mg/kg, s.c.). Results showed that naloxone reversed its antinociceptive activity (Table no. 1).

Table I: Effect of isolated  $\beta$ -sitosterol, various extracts of *Oxalis corniculata* leaves and effect of naloxone on  $\beta$ -sitosterol isolated from PEOC by hot plate test.

Treatment	Reaction time (s)					
	Time after treatment (min)					
	0	30	60	90	120	150
Control	2.4 $\pm$ 0.4	2.9 $\pm$ 0.3	2.5 $\pm$ 0.4	2.7 $\pm$ 0.5	2.2 $\pm$ 0.2	2.9 $\pm$ 0.3
Pentazocine (10 mg/kg, i.p.)	2.9 $\pm$ 0.5	7.5 $\pm$ 0.4*	12.0 $\pm$ 0.5*	10.3 $\pm$ 0.4*	6.2 $\pm$ 0.3*	3.5 $\pm$ 0.4
PEOC (100 mg/kg, i.p.)	2.3 $\pm$ 0.3	5.5 $\pm$ 0.4*	8.4 $\pm$ 0.4*	8.3 $\pm$ 0.3*	6.0 $\pm$ 0.4*	3.3 $\pm$ 0.4
CFOC (100 mg/kg, i.p.)	2.3 $\pm$ 0.6	4.9 $\pm$ 0.3*	7.4 $\pm$ 0.6*	6.9 $\pm$ 0.4*	4.2 $\pm$ 0.4	3.5 $\pm$ 0.2
EAOC (100 mg/kg, i.p.)	2.5 $\pm$ 0.4	4.5 $\pm$ 0.5	6.5 $\pm$ 0.4*	7.8 $\pm$ 0.2*	4.2 $\pm$ 0.5	3.9 $\pm$ 0.2
MEOC (100 mg/kg, i.p.)	2.3 $\pm$ 0.3	4.3 $\pm$ 0.5	6.2 $\pm$ 0.2*	6.5 $\pm$ 0.5*	3.9 $\pm$ 0.4	2.9 $\pm$ 0.4
$\beta$ -sitosterol (5 mg/kg, i.p.)	2.4 $\pm$ 0.4	4.2 $\pm$ 0.3	6.9 $\pm$ 0.3*	7.7 $\pm$ 0.4*	5.2 $\pm$ 0.3	2.9 $\pm$ 0.5
$\beta$ -sitosterol (10 mg/kg, i.p.)	2.3 $\pm$ 0.5	5.2 $\pm$ 0.2*	8.5 $\pm$ 0.5*	9.3 $\pm$ 0.5*	6.2 $\pm$ 0.3*	3.9 $\pm$ 0.4
$\beta$ -sitosterol (20 mg/kg, i.p.)	2.2 $\pm$ 0.3	6.3 $\pm$ 0.5*	9.8 $\pm$ 0.4*	11.1 $\pm$ 0.3*	8.2 $\pm$ 0.2*	4.3 $\pm$ 0.3
Pentazocine (10 mg/kg, i.p.) + naloxone (1 mg/kg, s.c.)	2.4 $\pm$ 0.4	2.5 $\pm$ 0.3	2.4 $\pm$ 0.4	2.5 $\pm$ 0.5	2.6 $\pm$ 0.2	2.5 $\pm$ 0.3
$\beta$ -sitosterol (10 mg/kg, i.p.) + naloxone (1 mg/kg, s.c.)	2.5 $\pm$ 0.4	2.5 $\pm$ 0.3	2.6 $\pm$ 0.4	2.6 $\pm$ 0.5	2.5 $\pm$ 0.2	2.5 $\pm$ 0.3

All the values are expressed as mean  $\pm$  SEM; n = 6; \*  $P < 0.05$  significant compared to control

### 3.3 Acetic acid-induced writhing test

Petroleum ether, chloroform and ethyl acetate extracts (100 mg/kg, i.p.) produced significant inhibition of writhing reaction induced by acetic acid as compared to the control group.  $\beta$ -sitosterol (5, 10 and 20 mg/kg, i.p., each) isolated from petroleum ether extract showed comparable activity with standard drug paracetamol, 50 mg/kg, i.p. and the activity was dose dependent (Table 2).

**Table 2 Effect of isolated  $\beta$ -sitosterol and various extracts of *Oxalis corniculata* on acetic acid-induced writhing on mice**

Treatment	Number of writhings
Control	66.17 $\pm$ 1.7
Paracetamol (50 mg/kg, i.p.)	33.33 $\pm$ 2.9*
PECO (100 mg/kg, i.p.)	43.14 $\pm$ 1.9*
CFOC (100 mg/kg, i.p.)	47.12 $\pm$ 2.2*
EAO (100 mg/kg, i.p.)	52.5 $\pm$ 2.3*
MEOC (100 mg/kg, i.p.)	55.12 $\pm$ 1.8
$\beta$ -sitosterol (5 mg/kg, i.p.)	39.54 $\pm$ 3.0*
$\beta$ -sitosterol (10 mg/kg, i.p.)	36.12 $\pm$ 1.6*
$\beta$ -sitosterol (20 mg/kg, i.p.)	34.21 $\pm$ 1.4*

All the values are expressed as mean SEM; n = 6, \* P < 0.05 significant compared to control group.

### 3.4 Anti-inflammatory activity

In the acute inflammation model, i.e., carrageenan-induced rat paw edema method, petroleum ether, chloroform and ethyl acetate extracts produced significant (P < 0.05) inhibition of paw edema as compared to the control.  $\beta$ -sitosterol (5, 10 and 20 mg/kg, i.p., each) isolated from petroleum ether extract showed comparable activity with standard drug ibuprofen (50 mg/kg, i.p.) and the activity was dose dependent (Table 3).

**Table 3: Effect of isolated  $\beta$ -sitosterol and various extracts of *Oxalis corniculata* on carrageenan-induced rat paw edema**

Treatment	Mean increase in paw volume (ml) $\pm$ SEM				
	Time in minutes				
	0	30	60	90	120
Carrageenan (control)	0.29 $\pm$ 0.06	0.53 $\pm$ 0.08	0.83 $\pm$ 0.14	0.90 $\pm$ 0.17	0.94 $\pm$ 0.19
Ibuprofen (50 mg/kg, i.p.)	0.29 $\pm$ 0.09	0.36 $\pm$ 0.12*	0.35 $\pm$ 0.12*	0.32 $\pm$ 0.11*	0.31 $\pm$ 0.18*
PECO (100 mg/kg, i.p.)	0.29 $\pm$ 0.19	0.41 $\pm$ 0.14	0.40 $\pm$ 0.12*	0.37 $\pm$ 0.14*	0.35 $\pm$ 0.17*
CFOC (100 mg/kg, i.p.)	0.30 $\pm$ 0.14	0.41 $\pm$ 0.12	0.40 $\pm$ 0.14*	0.40 $\pm$ 0.12*	0.37 $\pm$ 0.16*
EAO (100 mg/kg, i.p.)	0.30 $\pm$ 0.18	0.42 $\pm$ 0.22	0.41 $\pm$ 0.14*	0.40 $\pm$ 0.07*	0.37 $\pm$ 0.09*
MEOC (100 mg/kg, i.p.)	0.30 $\pm$ 0.12	0.46 $\pm$ 0.07	0.53 $\pm$ 0.06	0.56 $\pm$ 0.17	0.47 $\pm$ 0.18
$\beta$ -sitosterol (5 mg/kg, i.p.)	0.29 $\pm$ 0.07	0.39 $\pm$ 0.08*	0.39 $\pm$ 0.12*	0.37 $\pm$ 0.17*	0.34 $\pm$ 0.22*
$\beta$ -sitosterol (10 mg/kg, i.p.)	0.29 $\pm$ 0.08	0.37 $\pm$ 0.12*	0.38 $\pm$ 0.12*	0.37 $\pm$ 0.11*	0.32 $\pm$ 0.18*
$\beta$ -sitosterol (20 mg/kg, i.p.)	0.29 $\pm$ 0.17	0.37 $\pm$ 0.06*	0.37 $\pm$ 0.08*	0.34 $\pm$ 0.12*	0.32 $\pm$ 0.06*

All the values are expressed as mean SEM; n = 6, \* P < 0.05 significant compared to control group

## 4. Discussion

The hot plate test is the specific central antinociceptive test. [16]  $\beta$ -sitosterol isolated from petroleum ether extract showed significant results in this test, so there may be involvement of opioid receptors. The opioid agents exert their analgesic action via the supraspinal ( $\mu_1$ ,  $k_3$ ,  $\delta_1$ ,  $\sigma_2$ ) and spinal ( $\mu_2$ ,  $k_1$ ,  $\delta_2$ ) receptors. [17] To check opioid effect of isolated  $\beta$ -sitosterol, various extracts of *Oxalis corniculata* leaves and effect of naloxone on  $\beta$ -sitosterol isolated from PEOC on thermic stimulus-induced pain (hot plate test) involvement in the mechanism of antinociceptive action, an opioid antagonist, naloxone, was used. [18] The interaction between naloxone and  $\beta$ -sitosterol isolated from petroleum ether extract of *Oxalis corniculata* leaves exerted the possible mechanism of central analgesic activity on the pain threshold of mice. Results showed that the naloxone reversed its antinociceptive activity. Therefore, it is possible that the  $\beta$ -sitosterol isolated from petroleum ether extract exerts its effect through the central opioid receptor or promoted release of endogenous opioid peptides.

Intraperitoneal injection of acetic acid produced pains through activation of chemosensitive nociceptors. or irritation of the visceral surface, which led to liberation of histamine, bradykinins, prostaglandins and serotonin. [19] Thus, the antinociceptive activity of opioid partial agonist and non-steroidal anti-inflammatory agents can be determined

by the writhing test. [20] The mechanism of analgesic effect of  $\beta$ -sitosterol isolated from petroleum ether extract of *Oxalis corniculata* leaves could probably be due to blockage of effect or release of endogenous substances that excite pain nerve endings. Overall,  $\beta$ -sitosterol isolated from petroleum ether extract of *Oxalis corniculata* leaves showed potent antinociceptive activity in both the tests. Prostaglandins and bradykinins were suggested to play an important role in analgesia. [21]

Carrageenan-induced edema is a biphasic response. In the first phase mediator are through the release of serotonin, histamine and kinins, whereas the second phase is related to the release of prostaglandin and slow reacting substances which peak at 3 h. [22] In case of analgesia, prostaglandins and bradykinins were suggested to play an important role in the pain process. [23] Some sterols and triterpenes are responsible for anti-inflammatory and analgesic activity. [24]

From this, we can conclude that  $\beta$ -sitosterol isolated from petroleum ether extract of *Oxalis corniculata* leaves has analgesic and anti-inflammatory action; it works through central mechanism through opoid receptors.

## Declaration of interest

The authors report that they have no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

## References

- [1] Goyal BR, Goyal RK, Mehta AA. *Pharmacognosy Reviews*, 2007; 1: 143-150.
- [2] Rastogi RP, Malhotra BN. *Compendium of Indian medicinal plants*. Lucknow: CDRI Publication and Information Directorate; 1984.
- [3] Kirtikar KR, Basu BD, *Indian Medicinal Plants*. Dehradun, India: International Book Distributors; 1991.
- [4] Nadkarni KM. *Indian Materia Medica*. Bombay: Popular Prakashan Pvt. Ltd.; 1982.
- [5] Gaitonde BB, Jogalekar SN, Kulakarni HJ. Anti-inflammatory activity of *Oxalis corniculata* in carrageenan induced paw oedema in rats. *Journal of Research in Indian medicine*, 1977; 12: 12.
- [6] Taranalli SV, Tipare SV, Torgal SS. Wound Healing activity of *Oxalis corniculata* whole plant extract. *Indian Journal of Pharmaceutical Sciences*, 2004; 66: 444-446.
- [7] Raghavendra MP, Satish S, Raveesha KA. Phytochemical analysis and antibacterial activity of *Oxalis corniculata*. *My Science*, 2006; 1:72-78.
- [8] Ackola KJ, Mwangi JW. Smooth muscle relaxant, cardio relaxant, hypotensive activity of *Oxalis corniculata*. *Int J Pharmacog*, 1995; 33: 247-249.
- [9] Sharma RA, Kumara A. Photochemistry, Pharmacology and Therapeutic application of *Oxalis corniculata*; A Review. *Int J Pharm Pharm Sci*, 2014; 6 (3): 6-12.
- [10] Srikanth M, Tadigotla S, Veeresh B. Phytochemistry and pharmacology of *Oxalis corniculata* Linn. A review. *IJPSR* 2012; 11: 4077-4085.
- [11] Pal S, Sen T, Nag Chauduru, AK. Neuropsychopharmacological profile of the methanolic fraction of leaf extract *Bryophyllum pinnatum*. *J Pharm Pharmacol*, 1999; 51: 313-318.
- [12] Brune K, Alpermann H. Non-acidic inhibition of prostaglandin production, carrageenine oedema and yeast fever. *Ag action*, 1983; 13: 360-363.
- [13] Asongalem EA, Foyet HS, Ngogang J. Analgesic and anti-inflammatory activities of *Erigeron floribundus*. *J Ethnopharmacol*, 2004; 91: 301-308.
- [14] Koster R, Anderson M, De Beer EJ. Acetic acid for analgesic screening. *Fed Proc*, 1959; 18: 412-418.
- [15] Winter CA, Risley EA, Nuss GW. Carrageenin-induced edema in hind paw of the rat as an assay for antiinflammatory drugs. *Proc Soc Expt Biol Med*, 1962; 111: 544.
- [16] Parkhouse J, Pleuvry BJ. *Analgesic drug*, Oxford: Blackwell 1979.
- [17] Reisine T, Pasternack G. Opioid analgesics and antagonists. In: Hardman JG, LE Limbird, ed. *Goodman and Gilman's, the pharmacological basis of therapeutics*, New York: McGraw-Hill 1996; 9: p. 5216.
- [18] Nirmal SA, Pal SC, Mandal SC. Analgesic and anti-inflammatory activity of  $\beta$ -sitosterol isolated from *Nyctanthes arbortristis* leaves. *Inflammopharmacol*, 2012; 20: 219-224.
- [19] Stai HY, Chen YF, Wu TS. Anti-inflammatory and analgesic activities of extract from roots of *Angelica pubescens*. *Planta Med*, 1995; 61: 1-8.
- [20] Garcia MD, Fernandez MA, Alvarez A. Antino-ciceptive and anti-inflammatory effect of the aqueous extract from leaves of *Pimenta racemosa* var. *ozua* (Mirtaceae). *J Ethanopharmacol*, 2004; 91: 2973.
- [21] Nguetefack TB, Nanab P, Atsamoa AD. Analgesic and anticonvulsant effect of extracts from leaves of *Kalanchoe crenata* (Andrews) Haworth (Crassulaceae). *J Ethanopharmacol*, 2006; 106: 70-75.
- [22] Dray A, Perkin M. Bradykinin and inflammatory pain. *Trends Neurosci*, 1993; 16: 99-104.
- [23] Vinegar R, Schreiber W, Hugo R. Biphasic development of carrageenan oedema in rats. *J Pharmacol Exp Ther*, 1969; 166: 96-103.
- [24] Singh S, Bani S, Singh GB. Anti inflammatory activity of lupeol. *Fitoterapia*, 1997; 68: 9-16.