In-vivo and in-vitro screening of medicinal plants for their anti-inflammatory activity: an overview

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ABSTRACT

Despite the progress made in medical research for the past decades, the treatment of many serious diseases is still problematic. Inflammation is the response of living tissues to injury. It involves a complex array of enzyme activation, mediator release, extravasations of fluid, cell migration, tissue breakdown and repair. Inflammation has become the focus of global scientific research because of its implication in virtually all human and animal diseases. As a result of adverse effects such as gastric lesions caused by non-steroidal anti-inflammatory drugs (NSAID), tolerance and dependence induced by opiates, the use of these drugs as anti-inflammatory agents have not been successful in all cases. Therefore, new anti-inflammatory drugs lacking these side effects are being researched as alternatives to NSAID and opiates. Attention is being focused on the investigation of the efficacy of plant-based drugs used in the traditional medicine because they are cheap, have little side effects. Hence, in the present review the various animal models used for preclinical screening anti-inflammatory activity herbs was compiled.

Keywords: Inflammation, Animal Models, Plant Extract, Mechanism of action.

INTRODUCTION

Inflammation is part of the complex biological response of vascular tissues to harmful stimuli, such as pathogens, damaged cells, or irritants. Inflammation is a protective attempt by the organism to remove the injurious stimuli and to initiate the healing process. Inflammation is not a synonym for infection, even in cases where inflammation is caused by infection. Although infection is caused by a microorganism, inflammation is one of the responses of the organism to the pathogen. Without inflammation, wounds and infections would never heal. Similarly, progressive destruction of the tissue would compromise the survival of the organism (Wikipedia). The plants are one of the most important sources of medicines. India is known due to availability of several thousands of medicinal plants in the different bioclimatic zones anti-inflammatory diseases (Hemamalini et al., 2010).
DIFFERENT MODELS USED TO STUDY INFLAMMATION

Acetic acid induced vascular permeability (Lee et al., 2009).

**Plant used:** Asparagus cochinchenisns.
**Family:** Liliaceae.
**Part used:** Dried and pulverized roots.
**Common name:** Asparagus root, shiny asparagus.
**Solvent:** 70% ethanol.
**Yield:** Not mentioned.
**Dose:** 2 g/kg.
**Route of administration:** Orally
**Chemical used:** Indomethacin, Evans blue dye, Acetic acid.

**Procedure**

Acetic acid-induced vascular permeability in ICR mice was performed as described previously. Briefly, 1 h after oral administration of ACE (200 mg/kg), indomethacin (5 mg/kg), or an equivalent volume of vehicle (3%, v/v Tween 80), 0.2 ml of Evans blue dye (0.25% in normal saline) was administered intravenously through the tail vein. Thirty minutes later, the animals received 1 ml/100 g of acetic acid (0.6%, v/v) i.p. Treated animals were sacrificed 30 min after acetic acid injection and the peritoneal cavity washed with normal saline (3 ml) into heparinized tubes and centrifuged. The dye content of the supernatant was measured at 610 nm using a microplate reader (molecular device). The results were expressed as arbitrary units of relative value.

**Mechanism of action**

The anti-inflammatory activity of *A. cochinchenisns* with 70% ethanol extract may be due to blockade of pro-inflammatory cytokine production, neutrophil-mediated myeloperoxidase activity, inhibition of IL-1β and TNF-α and to the subsequent blockade of leukocyte accumulation.

**Conclusion**

These results demonstrate that ACE is an effective anti-inflammatory agent in murine phorbol ester-induced dermatitis, and suggest that the compound may have therapeutic potential in a variety of immune-related cutaneous diseases.

**Carrageenan – induced oedema.** (Ilavarasan et al., 2005).

**Plant used:** Cassia fistula Linn.
**Family:** Caesalpinaceae.
**Part used:** Bark.
**Common name:** Amaltas.
**Solvent:** Water and methanol.
**Yield:** Water- 7% w/w and methanol- 9% w/w.
**Dose:** 2000 mg/kg.
**Route of administration:** Orally.
**Chemical used:** Diclofenac sodium.

**Procedure**

Paw oedema was induced by injecting 0.1 ml of 1\% Carrageenan in physiological saline into the subplantar tissues of the left hind paw of each rat. The extracts CFA (*C. fistula Aqueous*), CFM (*C. fistula Methanolic*) were administered orally 30 min prior to Carrageenan administration. The paw volume was measured at 60, 120, 180, 240, minutes by the mercury displacement method using a plethysmograph. The percentage inhibition of paw volume in drug treated group was compared with the control group. Diclofenac sodium was used as reference standard.

**Mechanism of action**

The activity of *C. fistula* Linn. with aqueous and methanolic extracts may be due to inhibition of the mediators of inflammation such as histamine, serotonin and prostaglandin.

**Conclusion**

Plants which belong to *Caesalpinaceae* family are rich in flavonoids and bio flavonoids are known for their anti-inflammatory and antioxidant activities. Further research is in progress to identify the biomolecules responsible for the anti-inflammatory and antioxidant activities.

**Carrageenan induced air pouch model** (Paschapur et al., 2009.)

**Plant used:** Borassus flabellifer Linn.
**Family:** Areaceae.
**Part used:** Male flowers.
**Common name:** Palmyra palm, toddy or wine palm.
**Solvent:** Ethanol.
**Yield:** Not mentioned.
**Dose:** 150 and 300 mg/kg.
**Route of administration:** Orally.
**Chemical used:** Pure Diclofenac Sodium.

**Procedure**

The rats were divided into four groups. Rats were anesthetized and air cavities were produced by subcutaneous injection of 20 ml of sterile air into the intrascapular area of the back. An additional 10 ml of air was injected into the cavity every 3rd day to keep the space open. On the 7th day, 2 ml of 1% solution of carrageenan dissolved in saline was injected directly into the pouch to induced an inflammatory response. The rats were orally pre-treated with either vehicle or extract or diclofenac sodium 3 h prior to the injection of carrageenan. The second dose of treatment was repeated after 24 h of the first treatment. 48 h after carrageenan injection, the rats were anesthetized with ether and the pouch was carefully opened by a small incision. The volume of exudates was collected and measured. An aliquot of the exudate was used for quantification of leukocyte concentration using a haemocytometer and differential cell count was performed using a manual cell counter after staining with Wright’s stain. The results were expressed as the total number of neutrophil’s and monocytes.

**Mechanism of action**

The anti-inflammatory activity of *B. flabellifer* Linn. may be due to inhibiting either release of lysosomal enzymes or by stabilizing the lysosomal membrane, which is one of the major events responsible for the inflammatory process.
Conclusion

Plants which belong to Caesalpinaceae family are rich in flavonoids and bio flavonoids are known for their anti-inflammatory and antioxidant activities. Further research is in progress to identify the biomolecules responsible for the anti-inflammatory and antioxidant activities.

Carrageenan-induced pleurisy in rats (Badilla et al., 2003).

**Plant used:** Loasa speciosa.
**Family:** Loasaceae.
**Part used:** Leaves.
**Common name:** Campana.
**Solvent:** Water.
**Yield:** Not mentioned.
**Dose:** 250–500 mg/kg.
**Route of administration:** Intraperitoneally.
**Chemical used:** Indomethacin.

**Procedure**

Groups of six rats each were pretreated with the test extract (250 or 500 mg/kg, i.p.), indomethacin (10 mg/kg, i.p.) or saline (0.1 ml). One hour later all animals received an intrapleural injection of carrageenan (0.25 ml of 1% solution in 0.9% saline) on the right side of the thorax. Three hours later the animals were anaesthetized with ether and killed by bleeding through the portal vein. The pleural exudate was collected and the pleural cavity was washed with 1.0 ml saline containing heparin (10 IU/ml). The number of migrating leukocytes in the exudate was determined with a Neubauer chamber. Results were expressed as mean + S.E.M. of exudate pleural volumes (ml) and of total leukocytes.

Mechanism of action

The aqueous extract of *L. speciosa* leaves showed an inhibitory effect on leukocyte migration, and a reduction on the pleural exudates.

Conclusion

When given intraperitoneally, has analgesic and anti-inflammatory activities, which are dose-dependent over a range of 125–500 mg/kg. Further studies are necessary to assess the potential clinical use of this plant, or its extract or active principles, as anti-inflammatory and or analgesics.

Carrageenin- and arachidonic acid-induced paw edema (Ghule et al., 2006.).

**Plant used:** Lagerasia siceraria.
**Family:** Cucurbitaceae.
**Part used:** Fresh fruits.
**Common name:** Bottle gourd.
**Solvent:** Stand. fruit juice.
**Yield:** 22.5 % w/w.
**Dose:** 300 mg/kg.
**Route of administration:** Orally.
**Chemical used:** Arachidonic acid.

**Procedure**

Male rats weighing between 100-150 g were used. Paw edema was induced by an intradermal injection of carrageenin (1% in normal saline solution) or arachidonic acid (0.5% in 0.2 M carbonate buffer, pH 8.4) into the plantar surface of the right hind paw of the rats, at a volume of 0.05 or 0.1 ml, respectively. The edema volume was determined using a plethysmometer prior to and 1, 3 and 5 h after carrageenin injection, or 1 h after arachidonic acid injection. Test drugs were given 1 h prior to carrageenin or 2 h prior to arachidonic acid injection.

Mechanism of action

The fruit juice extract of *L. siceraria* has a good predictive value to screen anti-inflammatory agents. Inflammatory mediators such as kinin, serotonin, and PGs are released by EPP. It was found that the LSFJE elicited significantly inhibitory effect on the edema formation at all assessment times. Phenylbutazone, a COX-inhibitor, showed a marked reduction of the ear edema.

**Cotton pellet induced granuloma** (Ilavarasan et al., 2005.)

**Plant used:** Cassia fistula Linn.
**Family:** Caesalpinaceae.
**Part used:** Bark.
**Common name:** Amalltas.
**Solvent:** Water and methanol.
**Yield:** Water- 7% w/w and methanol- 9% w/w.
**Dose:** 2000 mg/kg.
**Route of administration:** Orally.
**Chemical used:** Diclofenac sodium.

**Procedure**

Wistar albino rats (170-200 gm) of either sex were divided into 4 groups of 6 animal in each group. Cotton pellets weighing 30+ 1mg were autoclaved and implanted subcutaneously into both sides of the groin region of each rat, Group I served as control and received the vehicle. The Extracts CFA and CFM at concentration 500mg/kg orally for Group II and III animals for same period. On the 8th day the animals were sacrificed and the pellets together with the granuloma tissues were carefully removed, dried in an oven at 60°C, weighed and compared with control. Diclofenac sodium (5 mg / kg / p.o.) was used as reference standard.

Mechanism of action

The anti-inflammatory activity of *C. fistula* Linn. With aqueous and methanolic extracts may be due to inhibition of the mediators of inflammation such as histamine, serotonin and prostaglandin.
Conclusion

Plants which belong to Caesalpinaceae family are rich in flavonoids and bioflavonoids are known for their anti-inflammatory and antioxidant activities.

Croton oil-induced mouse ear edema (Canigueral et al., 1998).

**Plant used:** Anthurium cerrocampanense.
**Family:** Araceae.
**Part used:** Whole plant.
**Common name:** Tailflower, anthrion, flamingo flower.
**Solvent:** Water, Ethanol, dichloromethane.
**Yield:** Dichloromethane-1%, ethanol- 1.34%, Water-4.7%.
**Dose:** 100mg/kg.
**Route of administration:** Intrapertitoneally.
**Chemical used:** Indomethacin.

Procedure

Groups of 10 animals were formed. Each animal was anesthetized with ketamine. After 5 min, each animals received 15 µl of a solution of croton oil in acetone or ethanol 43%, on the inner surface of the right ear. The extracts and reference drug were dissolved in the solution of croton oil. Five and a half hours after the administration of croton oil, the animals were sacrificed by cervical dislocation, and a 7 mm diameter disc from each ear was removed with a stainless steel punch. The edema size was determined in relation to the weight of untreated left ear.

Mechanism of action

The inflammatory process is caused by the release of mediators from tissues and migrating cells, and most strongly implicated are the prostaglandines (PGs), leucotrienes (LTs), histamine, bradykinin, platelet-activating factor (PAF) and interleukin-1.

Conclusion

activity is related to hystamine and serotonin mediators (Nishida et al., 1979; Nishida and Tomizawa, 1980). It is known that on arachidonic acid-induced rat paw edema, araquidonic acid derivatives, specially leucotriens, have an important role and the COX inhibitors show low or no activity.

Cutaneous inflammation induced to the inner surface of right ear (Manga et al., 2004).

**Plant used:** Alchornea cordifolia.
**Family:** Euphorbiaceae.
**Part used:** Leaves.
**Common name:** Christmas bush.
**Solvent:** Methanol.
**Yield:** 13.08% w/w.
**Dose:** 2000µg/g/cm².
**Route of administration:** Topically.
**Chemical used:** Indomethacin.

Procedure

Cutaneous inflammation was induced to the inner surface of the right ear (surface: about 1 cm²) of anaesthetized mice (145 mg/kg ketamine hydrochloride, intraperitoneally) by application of 15 µl of acetone or acetone–water (1:1) solutions containing 80 µg of Croton oil as irritant (control animals). For treated animals, appropriate amounts of indomethacin (reference drug) or of the tested extracts were dissolved in the Croton oil containing solution and applied as for controls. After 6 h, mice were sacrificed and a punch (5mm of diameter) was excised from both ears. Inflammation was measured as oedema formation and quantified by the weight difference between the treated and the untreated (opposite) ear samples.

Mechanism of action

The anti inflammatory activity of methanolic extract of A. cordifolia may reduced the inflammation in to the inner surface of the right ear.

Egg white induced hind paw edema (Arunachalam et al., 2009).

**Plant used:** Eclipta prostrata L.
**Family:** Astearaceae.
**Part used:** Leaves.
**Common name:** Trailing, Bhamgra.
**Solvent:** Methanol.
**Yield:** 8.7% w/w.
**Dose:** 100-200 mg/kg.
**Route of administration:** Orally.
**Chemical used:** Propylene glycol.

Procedure

Albino Wistar rats of either sex weighing about 160 - 180 g were divided into four groups of six animals each. The methanol extract of leaves of E. prostrata at 100 and 200 mgkg-1 was administered orally to first two groups of rats. The third and fourth group of rats received 5 mlkg⁻¹ propylene glycol as vehicle control or 8 mgkg⁻¹ cyproheptadine as drug control respectively, for comparative pharmacological assessment.

All the drugs and vehicle were given 1 h prior to the study. Freshly taken egg white (0.1 ml) was injected into the sub plantar tissue of the left hind paw of the rat. The volumes of the injected paws were measured at 0, 60, 120, 180 and 240 min using a plethysmometer. The percent increase in paw oedema of the treated group was compared with that of the control and the inhibitory effects of the drugs were studied.
Mechanism of action

The anti inflammatory activity of methanolic extract of *E. prostrata* L. has an inhibitory effect on the release of active pain substance such as histamine, serotonin, polypeptides or prostaglandins.

Conclusion

The preliminary phytochemical screening of leaves of *E. prostrata* indicated the presence of steroids, triterpenoids, flavanoids, tannins, reducing sugar and saponins. The steroids, alkaloids and triterpenoids present in the extract may be responsible for this anti-oedematosus effect.

Ethyl phenylpropionate-induced ear edema (Ghule *et al*., 2006.).

Plant used: *Lagenaria siceraria*.
Family: Cucurbitaceae.
Part used: Fresh fruits.
Common name: Bottle gourd.
Solvent: Stand. fruit juice.
Yield: 22.5 % w/w.
Dose: 300 mg/kg.
Route of administration: Orally.
Chemical used: Ethyl phenylpropionate.

Procedure

Male rats weighing 100-150 g were used. Ear edema was induced by topical application of EPP at a dose of 1 mg/20 μl per ear to the inner and outer surfaces of both ears by means of an automatic microliter pipette. Test drugs were applied topically in volumes of 20 μl just before the irritant. The control group received vehicle only. Before and at 30min, 1h and 2h after edema induction, the thickness of each ear was measured by vernier calipers. The percent inhibition of the edema formation of test substances was calculated.

Mechanism of action

The inflammatory activity appear to involve or depend on arachidonic acid release and metabolism and interaction with protein kinase. The fruit juice extract of *L. siceraria* has a good predictive value to screen anti inflammatory agents. Inflammatory mediators such as kinin, serotonin, and PGs are released by EPP. It was found that the LSFJE elicited significantly inhibitory effect on the edema formation at all assessment times. Phenylbutazone, a COX-inhibitor, showed a marked reduction of the ear edema.

Conclusion

EPP-induced ear edema test provides a skin inflammation model suitable for evaluation of topical and systemic anti-inflammatory agents. The majority of its activities appear to involve or depend on arachidonic acid release and metabolism and interaction with protein kinase C.

Formalin induced edema in rat paw (Hosseinzadeh., 2002.).

Plant used: *Crocus sativus Linn*.
Family: Iridaceae.
Part used: Powder of stigma and petal.
Common name: Saffron.
Solvent: Water and ethanol.
Yield: For water-50.8%/w/w and ethanol- 56.6%/w/w and for petal, water-15.5%/w/w and ethanol- 19%/w/w.
Dose: 0.8 g/kg and 2 g/kg.
Route of administration: Intraperitoneally.
Chemical used: Formaldehyde, Diclofenac.

Procedure

Rats were divided into groups of six. The inflammation was produced by subpeneurotic injection of 0.1 ml of 2% formaldehyde in the right hind paw of the first and third day. The animals were treated daily with the extracts or diclofenac intraperitoneally for 10 days. The daily changes in paw size were measured by wrapping a piece of cotton thread round the paw and measuring the circumference with a meter rule.

Mechanism of action

The petal extracts showed anti inflammatory activity in the chronic inflammation. The anti inflammatory activity of the petal extracts may be due to their content of flavonoids, tannins and anthocyanins which inhibites the cyclooxygenase activity.

Conclusion

We conclude that aqueous and ethanolic extracts of *E. prostrata* has an inhibitory effect on the release of active pain substance such as histamine, serotonin, polypeptides or prostaglandins.

Formalin-induced nociception in mice (Badilla *et al*., 2003).

Plant used: *Loasa speciosa*.
Family: Loasaceae.
Part used: Leaves.
Common name: Campana.
Solvent: Water.
Yield: Not mentioned.
Dose: 250–500 mg/kg.
Route of administration: Intraperitoneally.
Chemical used: Indomethacin.

Procedure

Each group of six mice each, was treated with the test extract (125, 250 and 500 mg/kg i.p. in saline solution), saline solution (i.p.) and indomethacin (10 mg/kg i.p.). One hour after treatment all animals were injected with 20 ml of 1% formalin in saline solution into the plantar surface of the left hind paw. Licking time was measured in the test chamber over 30 min, in two phases: the first phase was from time zero to 5 min after formalin injection.
and the second phase was from 20 to 30 min after formalin injection.

**Mechanism of action**

The aqueous extract of *L. speciosa* leaves showed an inhibitory effect on leukocyte migration, and a reduction on the pleural exudates.

**Conclusion**

When given intraperitoneally, has analgesic and anti-inflammatory activities, which are dose-dependent over a range of 125–500 mg/kg. Further studies are necessary to assess the potential clinical use of this plant, or its extract or active principles, as anti-inflammatories and or analgesics.

**Granuloma air pouch** (Ching., 2009).

- **Plant used:** Stereospermum kunthianum.
- **Family:** Bignoniaceae.
- **Part used:** Fresh stem bark
- **Common name:** Sansami, umana and alakiriti.
- **Solvent:** Water.
- **Yield:** 26.4 % w/w.
- **Dose:** 500 mg/kg.
- **Route of administration:** Intraperitoneally.
- **Chemical used:** Indomethacin.

**Procedure**

Wistar rats of either sex were randomly allotted into groups of five animals each. The dorsal skin surface of the rats was shaved and disinfected with 70% ethanol. Twenty millitres of air was injected subcutaneously under ether anaesthesia at the approximate midpoint of the animals’ back using a hypodermic syringe with the needle directed towards the scapular region. The animals were administered distilled water (5 ml/kg, p.o.), extract (400 mg/kg, p.o.), or indomethacin (10 mg/kg, s.c.). One hour later for the extract and thirty minutes for indomethacin treated animals respectively, 0.5 ml of carrageenan 10% w/v in olive oil was injected into the air pouch of each rat. Remnant air was removed from the air pouch 24 h after the injection of the carrageenan. The rats were treated daily with the same dose of extract or indomethacin for five days with the last dose on the fifth day given one hour prior to the time the animals were sacrificed. The animals were sacrificed by inhalation of excess chloroform. The air pouch was carefully opened and the volume of exudates formed in each animal was measured.

**Mechanism of action**

The aqueous extract of *S. kunthianum* stem bark possesses anti-inflammatory activity which is probably related to the inhibition of prostaglandin synthesis.

**Conclusion**

The aqueous extracts of *S. kunthianum* steam bark possessess anti-inflammatory activity, which is probably related to the inhibition of prostaglandin synthesis.

**Histamine-induced hind paw oedema** (Amresh 2007).

- **Plant used:** Fumaria indica.
- **Family:** Fumariaceae.
- **Part used:** Whole plant.
- **Common name:** Fumitory, pitpapra, khetpapra, parpata.
- **Solvent:** 50% ethanol.
- **Yield:** Not mentioned.
- **Dose:** 400 mg/ kg.
- **Route of administration:** Orally.
- **Chemical used:** Phenylbutazone.

**Procedure**

Right hind paw oedema was induced by the sub plantar injection of 0.1 ml of histamine. Extract and phenylbutazone were administered 1 h prior to the inflammatory insult. The paw volume compared to that negative control animal was recorded after 3 h and consider as anti-inflammatory response.

**Mechanism of action**

The caffeic acid and b-sitosterol may be responsible for the anti-inflammatory effects exhibited by *F. indica*. The ability of the *F. indica* extract in inflammatory activity may be due to the involvement of prostaglandins and other mediators in a different order of magnitudes.

**Conclusion**

Based on the present study, it can be concluded that *F. indica* has potential anti-inflammatory activity against both exudative and proliferative phases of inflammation. *F. indica* extract significantly raised the pain threshold. This offers a newperspective in the treatment of pain.

**Hot scald-induced rat paw edema** (Yin et al., 2000).

- **Plant used:** Boschnikia rossica.
- **Family:** Betulaceae.
- **Part used:** Whole plant.
- **Common name:** Bu Lao Cao.
- **Solvent:** Methanol extract was fractioned with CH2Cl2 and H2O. **Yield:** Not mentioned.
- **Dose:** 500-1000 mg/kg.
- **Route of administration:** Orally.
- **Chemical used:** BRH2O extract.

**Procedure**

Edema was induced on the right hind paw of rat by hot scald. The right hind paw of rat soaked in thermostat water bath main tained at 53 ±0.5 °C and cut-off time was 14 sec and test drug (500mg/kg of BRH2O extract) was given 30 minutes before the hot scald test. The volume of the right paw was measured before test and 1, 2, 3, 4, 5, 6 and 24 h after induction of inflammation.

**Mechanism of action**

* B. rossica extract exhibited inhibitory effect on formation of preneoplastic hepatic foci in early stage of rat chemical
hepatocarcinogenesis. Both CH\textsubscript{2}Cl\textsubscript{2} and H\textsubscript{2}O extracts from \textit{B. rossica} exerted anti-inflammatory effect in rats and mice.

**Conclusion**

\textit{B. rossica} extract exhibited inhibitory effect on formation of preneoplastic hepatic foci in early stage of rat chemical hepatocarcinogenesis. Both CH\textsubscript{2}Cl\textsubscript{2} and H\textsubscript{2}O extracts from BR exerted anti-inflammatory effect in rats and mice.

**HRBC membrane stabilization** (Jain et al., 2009).

- **Plant used:** \textit{Abutilon indicum} Linn.
- **Family:** Malvaceae.
- **Part used:** Leaves.
- **Common name:** Atibala.
- **Solvent:** Ethanol, chloroform and water.
- **Yield:** 26.4 % w/w.
- **Route of administration:** Not mentioned.
- **Chemical used:** Diclophenac, phosphate buffer, HRBC suspension.

**Procedure**

The HRBC membrane stabilization has been used as method to study the anti-inflammatory activity. Blood was collected from healthy volunteer. The collected blood was mixed with equal volume of sterilised Alsever solution (2\% dextrose, 0.8\% sodium citrate, 0.5\% citric acid and 0.42\% sodium chloride in water). The blood was centrifuged at 3000 rpm and packed cell were washed with isosaline (0.85\%, pH 7.2) and a 10\% (v/v) suspension was made with isosaline. The assay mixture contained the drug, 1 ml of phosphate buffer (0.15M, pH 7.4), 2 ml of hyposaline (0.36\%) and 0.5 ml of HRBC suspension. Diclophenac was used as reference drug. Instead of hyposaline 2 ml of distilled water was used in the control. All the assay mixture were incubated at 37\(\degree\)C for 30 min and centrifuged. The hemoglobin content in the supernatant solution was estimated using spectrophotometer at 560 nm. The percentage hemolysis was calculated by assuming the hemolysis produced in presence of distilled water of as 100\%.

**Mechanism of action**

HRBC membrane similar to lysosomal membrane components, the prevention of hypotonicity induced HRBC membrane lysis is taken as a measure of anti-inflammatory activity of drugs.

**Conclusion**

They increasing activity at low concentration levels but decreasing activity with high concentration. They have a critical concentration (50 mg/100ml) at which their activities are maximum. The activities of all extracts are comparable to that of Diclophenac at concentration of 50 mg/100ml. The variation of activity with time was studied at different concentration, the activities in general decreased with time.

**Human keratinocyte HaCaT cells** (Kim et al., 2009).

- **Plant used:** \textit{Acorus calamus} L.
- **Family:** Zingiberaceae.
- **Part used:** Leaves.
- **Common name:** Sweet flag.
- **Solvent:** Water.
- **Yield:** Not mentioned.
- **Dose:** 50 mg/kg.
- **Route of administration:** Intraperitoneally.
- **Chemical used:** Immunofluorescence staining, polyninosinic:polycytidylic acid.

**Procedure**

HaCaT cells treated with polyninosinic:polycytidylic acid (polyI:C) and peptidoglycan (PGN) induced the inflammatory reactions. The anti-inflammatory activities of ACL were investigated using RT-PCR, ELISA assay, immunoblotting, and immunofluorescence staining.

**Mechanism of action**

\textit{A. calamus} leaf extract inhibits the production of pro-inflammatory cytokines.

**Conclusion**

These results suggest that ACL inhibits the production of pro-inflammatory cytokines through multiple mechanisms and may be a novel and effective anti-inflammatory agent for the treatment of skin diseases.

**Leucocyte migration** (Ching et al., 2009).

- **Plant used:** \textit{Stereospermum kunthianum}.
- **Family:** Bignoniaceae.
- **Part used:** Fresh stem bark.
- **Common name:** Sansami, umana and alakiriti.
- **Solvent:** Water.
- **Yield:** 26.4 \% w/w.
- **Dose:** 500 mg/kg.
- **Route of administration:** Intraperitoneally.
- **Chemical used:** Indomethacin, Phosphate buffered saline.

**Procedure**

Rats were randomly allotted to groups of five animals per group. They were administered by oral route, distilled water (5 ml/kg), extract (400 mg/kg) or indomethacin (10 mg/kg) one hour before intraperitoneal injection of 0.1 ml of carrageenan, 1\%w/v in normal saline. Three hours later the rats were sacrificed by excess chloroform inhalation. An incision was made on the peritoneal cavity- of each rat and 5 ml of phosphate buffered saline was injected. After gentle massage of the peritoneum, the exudates was aspirated with a sterile syringe. The exudates volume as well as the total leucocyte count was determined.
Mechanism of action

The aqueous extract of Stereosperum kunthianum stem bark possesses anti-inflammatory activity which is probably related to the inhibition of prostaglandin synthesis.

Conclusion

Migration of leucocyte would not be directly related to cyclooxygenase products, but the process is inhibited by non-steroidal anti-inflammatory compounds indicating that many mechanisms may be implicated in its control. The inhibitory effects of the extract on the intraperitoneal formation of exudates and leucocytes mobilization are probably due to the inhibition of prostaglandins. This possibility is reinforced by the fact that the extract at the same dose (400 mg/kg) remarkably inhibited paw oedematous process which is believed to be mediated by prostaglandine.

LPS-Activated Raw264.7 Cells (Juhas et al., 2009).

Plant used:- Moutan cortex.
Family:- Paeoniaceae.
Part used:- Root cortex.
Common name:- Mudanpi.
Solvent:- Methanol.
Yield:- Not mentioned.
Dose:- 0.1 and 0.3 mg/ml.
Route of administration:- Orally.
Chemical used:- not mentioned.

Procedure

We treated LPS to Raw264.7 cells, collected media every 3 h for 24 h, detected cytokines from the collected media, and then determined appropriate time for each cytokine assay. TNF-α, IL-1β and IL-6 were highly induced by LPS at 12, 12 and 6 h, respectively (data are not shown). TNF-α, IL-1β and IL-6 from the culture media were analyzed at the appropriate time. 0.3 mg ml⁻¹ of MCE significantly reduced the level of TNF-α, IL-1β and IL-6 at 12, 12 and 6 h incubation. LPS-activated PGE₂ also decreased by MCE as compared to control. PGE₂ per 1 ml medium w-as 6.89 pg in control and increased to 48.6 pg in LPS group. However, PGE₂ was reduced to 30.2 and 14.5 pg ml⁻¹ in 0.1 and 0.3 mg ml⁻¹ of MCE, respectively.

Mechanism of action

The anti-inflammatory activity of methanolic extract of M. cortex (MCE) inhibited the production of NO and prostaglandin E₂ (PGE₂), the expression of inducible NO synthase (iNOS), cyclooxygenase-2 (COX-2) and phosphorylated inhibitor of kBa (p-IkBa), and the activation of nuclear factor kBa (NFkB). MCE also reduced the concentration of tumor necrosis factor-a (TNF-a), interleukin-1β (IL-1β) and interleukin-6 (IL-6) in the Raw264.7 cells that were activated by LPS.

Mechanism of action

The anti-inflammatory activity of aqueous extract of Rheedia longifolia may be due to the inhibition of release of chemical inflammatory mediators such as prostaglandins and cytokines.

Conclusion

M. cortex extract can have anti-inflammatory activity by suppressing the phosphorylation of I-kBa and the activation of NF-kB, and by inhibiting the expression of iNOS and COX-2 in LPS-activated Raw264.7 cells.

Mouse model of acute and chronic inflammation (Lee et al., 2009).

Plant used:- Asparagus cochinchinensis.
Family:- Liliaceae.
Part used:- Dried and pulverized roots.
Common name:- Asparagus root, shiny asparagus.
Solvent:- 70% ethanol.
Yield:- Not mentioned.
Dose:- 2 g/kg.
Route of administration:- Orally.
Chemical used:- Acetone, Indomethacin.

Procedure for acute model

The mouse model of acute inflammation employed here was a slight modification of a previously described Procedure. Edema was induced on the right ear by topical application of 2.5 µg/ear TPA (in 20_l acetone). To examine the effect of ACE on ear edema following intraperitoneal (i.p.) challenge, groups of mice were injected with ACE, vehicle (saline, negative control), or indomethacin (5 mg/kg, positive control) at 30 min prior to TPA challenge. Ear thicknesses and weights were measured 6 h after topical application of TPA.

Procedure for chronic model

The effect of ACE on chronic skin inflammation was evaluated by a slight modification of a previous described Procedure. Briefly, 20_l of a solution of TPA (2.5_µg/ear×6 times) or acetone (vehicle) were topically applied to the inner and outer ear surfaces of both ears of each mouse with a micropipette on alternate days. ACE (200mg/kg), vehicle (saline, negative control), or indomethacin (5 mg/kg, positive control) was given once a day (i.p.) for 10 days each morning immediately after TPA application. On day 10, the mice were sacrificed at 6 h after treatment, and 6-mm2 diameter ear punch biopsies were collected and weighed.

Mechanism of action

The anti-inflammatory activity of A. cochinchinensis with 70% ethanol extract may be due to blockade of pro-inflammatory cytokine production and neutrophil-mediated myeloperoxidase activity, inhibition of IL-1β and TNF-α and to the subsequent blockade of leucocyte accumulation.
Conclusion
These results demonstrate that ACE is an effective anti-inflammatory agent in murine phorbol ester-induced dermatitis, and suggest that the compound may have therapeutic potential in a variety of immune-related cutaneous diseases.

Neutrophil migration into peritoneal cavity
(Venegas-flores., 2002).

**Plant used:** Calea zacatechichi.
**Family:** Compositae/Asteraceae.
**Part used:** Leaves.
**Common name:** Dream herb, Calea.
**Solvent:** Water.
**Yield:** Not mentioned.
**Dose:** 100 and 10 mg/kg.
**Route of administration:** Intraperitoneally.
**Chemical used:** Indomethacin or dexamethasone.

Procedure
The rats groups were injected with 3 ml of carrageenan (100 µg/ml) prepared in sterile saline solution into the peritoneal cavity, and 4 h later the abdominal cavity was washed with phosphate buffered saline containing 5 U/ml of heparin (Sigma, St Louis, MO) and 5% of bovine serum albumin. The total cell counts were done in a Neubauer chamber and differential cell counts were performed by the Souza and Ferreira technique. One hour before the carrageenan injection, the rats groups were treated with 10 and 100 mg/kg po of the aqueous extract, saline (control), indomethacin or dexamethasone(10 and 1 mg/kg, po), respectively.

Mechanism of action
The Anti inflammatory activity of aqueous extract of *Calea zacatechichi* may be due to inhibition of prostaglandin synthesis.

Conclusion
Dose of dexamethasone used produced a higher inhibition of neutrophil migration than the effect produced by indomethacin, supporting the possible role of leukotrienes in the inflammation model. These results suggested that antiinflammatory activity showed by *C. zacatechichi* could be related to the biosynthesis of prostaglandins and lipoxygenase products.

**Paw edema induced by histamine and serotonin**
(Dimo et al., 2006).

**Plant used:** Kalanchoe crenata.
**Family:** Crassulaceae.
**Part used:** leaves.
**Common name:** Never die or dog’s liver.
**Solvent:** Methylene chloride/ methanol.
**Yield:** Not mentioned.
**Dose:** 600 mg/kg.
**Route of administration:** Orally.

**Chemical used:** Pyrilamine malate, Histamine, Serotonin.

**Procedure**
In another set of experiments histamine and serotonin were used as the phlogistic agents. The n-butanol fraction of *K. crenata* extrat and control vehicle were administered one hour before the injection of inflammatory mediators. The respective strength of the inflammatory mediators, The volume injected, and the time of determination of volume of edema are indicated in parentheses, serotonin and histamine. Pyrilamine maleate was used as the antagonist of histamine.

**Mechanism of action**
The methylene chloride/ methanol extracts of *K. crenata* and the aqueous fraction significantly inhibited paw edema induced by carrageenan in the first phase, suggesting an inhibitory effect on the release of histamine and serotonin. The n-butanol fraction showed significant inhibition of edema in all the three phases. Acute inflammation induced by formaline which provokes in production of endogenous mediators such as histamine, serotonin, prostaglandins and bradykinin.

**Conclusion**
*K. crenata* is an antiinflammatory and antiarthritic agent that blocks histamine and serotonin pathways.

**Paw oedema induced by egg albumin in rat**
(Gertsch et al., 2008).

**Plant used:** Securidaca longipedunculata.
**Family:** Polgalacea.
**Part used:** Fresh roots.
**Solvent:** Petroleum ether and methanol.
**Common name:** Uwar Maganinunar in Hausa and ezeogwu in Ibo.
**Yield:** Methanol extract-10.9%, pet. ether fraction-0.174% and methanol fraction-12.6%.
**Dose:** 50 mg/ear.
**Route of administration:** Applied topically.
**Chemical used:** Not mentioned.

**Procedure**
The methanol extract and methanol fraction Suppressed the development of paw edema by egg albumin in rats. The methanol extract evoked a non-dose related inhibition while the methanol fraction caused the reverse from 2 h. The petroleum ether fraction was did not exhibit anti-inflammatory activity.

**Mechanism of action**
Pharmacological screening of root bark extracts of *S. longipedunculata* has revealed that the root bark possesses potent anti-inflammatory effect in the topical and systemic models of acute inflammation. These extracts may have inhibited the release...
of pro-inflammatory mediators of acute inflammation such as histamine and prostaglandin.

**Conclusion**

These extracts may have inhibited the release of pro-inflammatory mediators of acute inflammation such as histamine and prostaglandin.

**PGE2 induced hind paw edema** (Kupeli et al., 2007).

*Plant used:* Geranium pretense subsp. Finitimum.
*Family:* Geraniaceae.
*Part used:* Aerial parts.

**Common name:** Woronouu.
**Solvent:** Water.
**Yield:** Not mentioned.
**Dose:** 0.5 mg/25µl.
**Route of administration:** Intraperitoneally.
**Chemical used:** ProstaglandinE2 in Tyroid’s solution.

**Procedure**

Sixty minutes after the oral administration of a test sample or dosing vehicle, each mouse was injected with fresh prepared suspension of PGE2 in Tyroid’s solution into subplantar tissue of the right hind paw. As the control, 5µl Tyroid’s solution was injected into that of the left hind paw. Paw edema was measured in every 15 min during a period of 75 min after the induction of inflammation.

**Mechanism of action**

The anti inflammatory activity of aqueous extract of Geranium pretense subsp. Finitimum may be due to the inhibition of production of prostaglandin. It also reduces the TPA induced mouse ear edema.

**Conclusion**

In this study revealed that the aerial parts of Geranium pretense subsp. Finitimum possess anti-inflammatory and antinociceptive properties and contribute a further support its use in traditional medicine for alleviating painful inflammatory conditions.

**Pleurisy induced by LPS in mice** (Frutuoso et al., 2007).

*Plant used:* Rheedia longifolia.
*Family:* Clusiaceae.
*Part used:* Leaves.
*Common name:* Bacupari.
*Solvent:* Water.
**Yield:** Not mentioned.
**Dose:** 50 mg/kg.
**Route of administration:** Intraperitoneally.
**Chemical used:** Aetic acid, cytosmears stained, May-Grunwald-Giemsza dye.

**Procedure**

The leaves aqueous extract of R. longifolia (50 mg/kg, i.p) was administered 1 h before the injection of LPS. Six hours after the injection of LPS the animals were sacrificed in a CO2 chamber, the thoracic cavity was opened and washed with 1 ml of PBS containing heparin 20 UI. The pleural wash was collected with the aid of a pipette and used to analyze the cellular infiltrate. The total number of leukocytes collected in pleural wash was evaluated in a Neubauer chamber after dilution of a pleural wash sample in 2% acetic acid. The differential analysis of leukocytes was accomplished in cytosmears stained with May-Grunwald-Giemsa dye. Each experimental group was performed with at least eight animals.

**Mechanism of action**

The anti inflammatory activity of aqueous extract of R. longifolia may be due to the inhibition of release of chemical inflammatory mediators such as prostaglandins and cytokines.

**Topical acute edema of the mouse ear** (Gertsch et al., 2008).

*Plant used:* Securidaca longipedunculata.
*Family:* Polgalacea.
*Part used:* Fresh roots.
*Common name:* Uwar Maganinunar in Hausa and ezeogwu in Ibo.
**Solvent:** Petroleum ether and methanol.
**Yield:** Methanol extract-10.9%, pet. ether fraction-0.174% and methanol fraction-12.6%.
**Dose:** 50 mg/ear.
**Route of administration:** Applied topically.
**Chemical used:** Not mentioned.

**Procedure**

The extract and fractions inhibited topical edema induced by xylem in the mouse ear. The fraction caused greater than the methanol extract in the order Petroleum ether fraction>Methanol fraction>Methanol extract.

**Mechanism of action**

Pharmacological screening of root bark extracts of S. longipedunculata has revealed that it possesses potent anti-inflammatory effect in the topical and systemic models of acute inflammation. These extracts may have inhibited the release of pro-inflammatory mediators of acute inflammation such as histamine and prostaglandin.
Conclusion
Pharmacological screening of root bark extracts of S. longipedunculata has revealed that the root bark possesses potent anti-inflammatory effect in the topical and systemic models of acute inflammation. These extracts may have inhibited the release of pro-inflammatory mediators of acute inflammation such as histamine and prostaglandin.

TPA-treated mouse ear edema (Hargrove et al., 2008).
- **Plant used:** Polygonum cuspidatum.
- **Family:** Polygonaceae.
- **Part used:** Root.
- **Common name:** Japanese knotweed or Mexican bamboo.
- **Solvent:** 50 % ethanol.
- **Yield:** Not mentioned.
- **Dose:** 2.5 mg/ear.
- **Route of administration:** Topically.
- **Chemical used:** 50% ethanol, Indomethacin.

Procedure
Edema was induced in both ears of each mouse by the topical application of 2 μg TPA dissolved in 20 μL of acetone to both the inner and outer ear surfaces. Thirty minutes after the application of TPA, the inner and outer surface of each ear was treated (10 μL to each side) with 50% ethanolic solutions of PCE in doses of 0.075, 0.15, 0.3, 1.25 and 2.5 mg PCE/ear (n = 8 at each dosage). Comparisons included equal volumes of 50% ethanol (vehicle control), indomethacin (0.5 mg/ear dissolved in 50% ethanol as an anti-inflammatory drug standard), or a 50%ethanol solution of trans-3, 5, 4'-trihydroxystilbene (resveratrol, 0.6 mg/ear). The thickness of each ear was measured using a micrometer before and at 4 h and 24 h after TPA administration. The micrometer was applied near the top of the ear distal to the cartilaginous ridges. At 24 h each animal was sacrificed with CO2 inhalation by the IACUC approved protocol. Ear punch biopsies (6 mm diameter hole punch) were taken immediately, weighed, frozen and stored at -80°C. A single investigator performed all ear measurements and biopsies in order to standardize the Procedure and reduce experimental error.

Mechanism of action
- **P. cuspidatum** extract inhibits development of edema and neutrophil infiltration in the TPA-treated mouse ear model of topical inflammation.

Conclusion
PCE inhibits development of edema and neutrophil infiltration in the TPA-treated mouse ear model of topical inflammation.

Xylene or croton oil-induced mouse ear edema (Yin et al., 2000).
- **Plant used:** Boschniakia rossica.
- **Family:** Betulaceae.
- **Part used:** Whole plant.

Procedure
An edema was induced on the right ear by topical application of xylene in mice 30 minutes after oral administration of 500mg/kg-1000mg/kg BR-H2O extract or BR-CH2Cl2 extract. The left ear was controled. Ear edema was measured by comparing the difference in weight (mg) between the same size of left and right ears 30 minutes after xylene induction and 4h after croton oil-induction of inflammation and swelling degree and inhibition rate were calculated.

Mechanism of action
- **B. rossica** extract exhibited inhibitory effect on formation of preneoplastic hepatic foci in early stage of rat chemical hepatocarcinogenesis. Both CH2Cl2 and H2O extracts from B. rossica exerted anti-inflammatory effect in rats and mice.

Conclusion
B. rossica extract exhibited inhibitory effect on formation of preneoplastic hepatic foci in early stage of rat chemical hepatocarcinogenesis. Both CH2Cl2 and H2O extracts from B. rossica exerted anti-inflammatory effect in rats and mice.
Mechanism of action

The stigma extracts showed activity against acute and chronic inflammation. The petal extracts showed anti-inflammatory activity in the chronic inflammation. The anti-inflammatory activity of the petal extracts may be due to their content of flavonoids, tannins and anthocyanins which inhibites the cyclooxygenase activity.

Conclusion

The aqueous and ethanolic extracts of saffron stigma and petal have an antinociceptive effect, as well as acute and/or chronic anti-inflammatory activity.

Zymosan-induced oedema in mice (Stefanova et al., 1995).

| Plant used: | Fraxinus ornus Linn. |
| Family:     | Oleaceae.            |
| Part used:  | Stem bark.           |
| Common name:| Flowering Ash, Manna, Manna Ash. |
| Solvent:    | 96% boiling ethanol. |
| Yield:      | Not mentioned.       |
| Dose:       | 5-15 mg/kg.         |
| Route of administration: | Intraperitoneally. |
| Chemical used: | 2% Zymosan.         |

Procedure

Odema in ICR mice was induced by injecting 0.025 ml of 2% Zymosan suspension in saline into the left hind paw. The right hind paw was used as a control and was injected with 0.025 ml of 0.9% saline. The animal were killed 3 h later, both hind paw cut off at the ankle and the difference between their weights calculated.

Mechanism of action

F. ornus bark contains several hydroxycoumarin derivatives, the main one being esculin (EN). The total ethanol extract from F. ornus bark contains substances of high potency capable of inhibiting classical pathway and alternative pathway complement activity. The comparison between the effects obtained with total ethanol extract and esculin in the haemolytic inhibitory assay indicates that the anticomplementary action of TE is not due only to EN.

Conclusion

Zymosan-induced AP activation of mouse serum in vitro is strongly suppressed by TE and EN. The effective dose of about 5-15 mg/kg is comparable to the data know for other lipoxygenase inhibitors like phenidone.

λ-Carrageenan (CARR) - induced paw edema (Huang et al., 2008).

| Plant used: | Hydrocotyle batrachium. |
| Family:     | Apiaceae.              |
| Part used:  | Whole plant.           |
| Common name:| Marshpennywort.        |
| Solvent:    | Water.                 |
| Yield:      | 26.37% w/w.            |
| Dose:       | 500 and 100 mg/kg.     |

Route of administration: - Orally.

Chemical used: - Indomethacin.

Procedure

The anti-inflammatory activity of HBW (Hydrocotyle batrachium Hance) was determined by the λ-Carrageenan-(CARR) induced edema test. Male ICR mice were randomly assigned to five groups and then fasted with free access to water for 24 h hours before the experiment. Fifty microliters of a 1% suspension of CARR in saline, which had been prepared 30 min before each experiments, was injected into the plantar side of the right hind paw of the mice. After 60 min, HBW at dose of 100, 500 and 1000 mg/kg were administrered orally, and after 90 min, indomethacin at the dose of 10 mg/kg was administered via an intraperitoneal route after the CARR treatment. Paw volume was measured prior to CARR injection and at 60, 120, 180, 240, 300, 360 min interval after the administration of the endematogenic agent using a plethysmometer. The degree of swelling was evaluated according to the a-b value, where a is the volume of the right hind paw after CARR treatment and b is the volume of the right hind paw before CARR treatment. Indomethacin was used as a positive control compound.

Mechanism of action

The anti-inflammatory activity of water extract of H. batrachium may be due to the inhibition of mediators of inflammation and also inhibites the synthesis of prostaglandin.

Conclusion

HBW appears to have analgesic and ant-inflammatory activities.

Carrageenan and dextran-induced pedal edema (Sarkar et al., 2005).

| Plant used: | Aloe vera. |
| Family:     | Asphodelaceae. |
| Part used:  | Leaves. |
| Common name:| Kumari, Musabbar. |
| Solvent:    | Dimethylsulfoxide. |
| Yield:      | Not mentioned. |
| Dose:       | Upto 25mg/kg. |
| Route of administration: | Orally. |
| Chemical used: | Dextran, Indomethacin. |

Procedure

Animals were divided into four groups (n = 6). In all the groups, acute inflammation was induced by injection of either 0.1 ml of freshly prepared carrageenan (1.0 %) in 0.9 % w/v NaCl solution or 0.1 ml of dextran (2%) in 0.9% w/v NaCl solution into the subplantar region of the hind paw of rats. AVL in different doses (0-25 mg/kg) and indomethacin (2.5, 5 and 10 mg/kg, as a standard reference) were orally administered one hour before injection of the phlogistic agent. The paw volumes were measured plethysmographically (using water) once prior to administration of the phlogistic agent and thereafter at hourly intervals for 3 h.
Mechanism of action

The anti-inflammatory activity that is mediated through antibradykinin activity and inhibition of prostaglandin production. A. vera leaf exudate also demonstrated that this anti-inflammatory activity is mediated partly via reduction of nitric oxide production in macrophages.

Conclusion

A. vera possesses acute and chronic antiinflammatory activity, which is partly mediated by reduced production of NO, which in turn prevents the release of inflammatory mediators.

Kaolin-induced paw oedema (Sevastre et al., 2007).

Plant used: Peucedanum officinale.

Family: Apiaceae.

Part used: Whole plant.

Common name: Hog's fennel.

Solvent: Not mentioned.

Yield: Not mentioned.

Dose: 25 mg/kg.

Route of administration: Orally.

Chemical used: kaolin injection.

Procedure

One hour later, suspension of kaolin 10% was intraplantary injected. The measurements, made by UGO BASILE 7140 digital plethysmometer, were done before kaolin injection (for assessing the initial volume of paw), and in 2, 4 and 24 hours after the injection. Inflammatory oedema represent the difference between the injected paw volume at 2, 4, respectively 24 hours and initial volume (IV). The inhibition of oedema (IO) represents the difference in paw volume, between treated animals (positive control group and experimental group) and untreated ones (negative control).

Mechanism of action

Peucedanum species contains mainly coumarins. Coumarins highly effective in the treatment of inflammatory oedema. It also acts as inhibitors of cyclooxygenase and 5-lipoxygenase. The Peucedanum extract have agonistic effect of histamine and down regulation of cyclooxygenase activity. It also inhibits the release of prostaglandin synthesis.

Conclusion

P. officinale has proved a significant antiinflammatory activity on kaolin induced rat paw oedema model, however the efficiency has been found lower than classic antiinflammatory therapy (phenylbutazone).

Lipopoly saccharide induced septic shock (Rao et al., 2007).

Plant used: Rhododendron dauricum Linn.

Family: Ericaceae.

Part used: Leaves.

Common name: Ezomurasaki shakunage.

Solvent: Water.

Yield: 16.2% w/w.

Dose: 200-500 mg/kg.

Route of administration: Orally.

Chemical used: D-galactosamine, Rhododendron dauricum L extracts, alanine, aspartate aminotransferase.

Procedure

In this, Number of deaths per group, Serum level of alanine aminotransferase, Serum level of aspartate aminotransferase. No deaths were recorded in the group of mice administered with only saline and D-galactosamine. However, in galactosamine primed mice injected with Lipopolysaccharide
(LPS), all the animals died before the completion of the experiment. The number of deaths in the group of animals pretreated with 10, 20, 40, and 80 mg/kg of the Rhododendron dauricum L. extracts prior to LPS-challenge were three, two, one and none, respectively. No deaths were recorded in the group of mice that received pentoxifylline (100 mg/kg). D-galactosamine injection before saline treatment resulted in serum level of 270.7 ± 3.2 U/ml and 304.8 ± 6.6 U/ml of alanine and aspartate aminotransferase respectively. In D-galactosamine primed mice injected with LPS, the levels elevated to 297.8 ± 3.5 U/ml and 335.8 ± 7.8 U/ml for alanine and aspartate aminotransferase respectively.

Mechanism of action
The exact Mechanism of action is not known.

Conclusion
The effect of R. dauricum L. extract was tested on induced dye leakage in the mouse skin. The effect of extract and pentoxyfylline were evaluated 2 hr after injection of LPS. The extract was found to produce inhibition of dye leakage to the same extent as pentoxyfylline. Subcutaneous injection of LPS on the back of mice and rats induced a plasma leakage at the site of injection and thus is used as a model of inflammation.

Hyaluronidase inhibitory assay (Hayati et al., 2007).

Plant used: Prismatomeris malayana.
Family: Rubiaceae.
Common name: Prismatomeris albidiflora King.
Part used: Root, stem and leaf.
Solvent: solution of leaf crud.
Yield: 9.84% w/v.
Dose: 200 mg/kg.
Route of administration: Orally.
Chemical used: Sodium chloride, Hyaluronic acid, Acetic acid.

Procedure
The assay medium consisting of 1.00 to 1.67 U
hyaluronidase in 100 μl 20 mM sodium phosphate buffer pH 7.0
with 77 mM sodium chloride and 0.01% Bovine Serum Albumin
(BSA) was pre-incubated with 5 μl of the test compound in DMSO
(dimethyl sulphoxide) for 10 min at 37 °C. Then the assay was
commenced by adding 100 μl hyaluronic acid (0.03%
300 mM sodium phosphate, pH 5.35) to the incubation mixture and
incubated for a further 45 min at 37°C. The undigested hyaluronic
acid was precipitated with 1 ml acid albumin solution made up of
0.1% bovine serum albumin in 24 mM sodium acetate and 79 mM
acetic acid, pH 3.75. After standing at room temperature for 10
min, the absorbance of the reaction mixture was measured at 600
nm. The absorbance in the absence of enzyme was used as the
reference value for maximum inhibition. The inhibitory activity of
test compound was calculated as the percentage ratio of the
absorbance in the presence of test compound vs. absorbance in the
absence of enzyme. The enzyme activity was checked by control
experiment that ran simultaneously, in which the enzyme was pre-
incubated with 5μl DMSO, followed by the assay Procedures
described above. In this case, the percentage ratio of the
absorbance in the presence of enzyme vs. that in the absence of
enzyme was in the range of 15 to 20%.

Mechanism of action
Hyaluronidase is an enzyme that degrades hyaluronic acid
and chondroitin sulfate which are components of the extra cellular
matrix of connective tissue. By degrading the components of
connective tissue, hyaluronidase promotes the spread of
inflammatory mediators throughout these tissues, thereby
contributing to the pathogenesis of inflammatory diseases such as
allergic effects, migration of cancer cells, inflammation and the
increase in permeability of vascular system.

Conclusion
The leaves (PML) showed the highest activity on
hyaluronidase inhibitory assay compared to the roots (PMR) and
stem (PMS).
SUMMARY AND CONCLUSION
The detail literature survey was done on various plants which can be used in inflammation including their plant used, family, part used, common name, solvent of extraction, yield, dose, route of administration, chemical used, Procedure Mechanism of action, and Conclusion was done. It is cleared from Mechanism of action of these extract that almost all drugs work on the principle of inhibition of prostaglandin and other inflammatory mediators synthesis.

REFERENCES