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Research Article

# Anti-inflammatory and Analgesic Properties of *Solanum melongena*

**Samane Jahanabadi[1], Bashir Ahmad[2], Vahid Nikoui[3], Gulkhubaz Khan[4], Muhammad Imran Khan[5]**

[1]Department of Pharmacology and Toxicology, Faculty of Pharmacy, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
[2]Department of Physiology, Bannu Medical College Bannu, KPK, Pakistan
[3]Razi Drug Research Center, Iran University of Medical Sciences, Tehran, Iran.
[4]Department of Pharmacy, Kohat University of Science and Technology, Kohat, KPK, Pakistan
[5]Department of Biomedical Sciences, Pak-Austria Fachhochschule: IAST, KPK, Pakistan.
*Correspondence: mik8782@gmail.com



## Abstract

*Solanum melongena* (SM), or eggplant, is a species of the nightshade family. In the traditional medicine system of the subcontinent, SM possesses excellent therapeutic effects on warts, burns, and many inflammatory diseases, such as stomatitis, arthritis, and gastritis. This study aimed to investigate the anti-inflammatory and analgesic effects of SM fruit. The anti-inflammatory effect was studied using carrageenan-induced edema in the rat's hind paw, while analgesic activity was studied by thermal and chemical induction of pain. Crude methanolic extract of the plant showed a potent analgesic effect. When used at doses of 10, 20, and 50mg/kg, SM caused significant inhibition ($P < 0.001$) of the nociception induced by acetic acid. In the formalin test, the fruit extract of SM (10, 20, and 50mg/kg i.p.) significantly ($P < 0.01$, $P < 0.001$) inhibited both phases of formalin-induced licking response in mice. In the hot plate assay, SM (50mg/kg i.p.) showed significant analgesic activity ($P < 0.01$, $P < 0.001$), similar to morphine. Furthermore, the methanolic extract of SM (10–50mg/kg i.p.) reduced the paw edema in the third hour after carrageenan administration, with maximum inhibition being 75% at 50mg/kg. We concluded that the crude methanolic extract of SM possesses analgesic and anti-inflammatory properties, which rationalize its traditional use in treating inflammatory conditions.

**Keywords**: *Peganum harmala*, cyclooxygenase, lipoxygenase, thromboxane, platelet aggregation, inflammation

## Introduction

Throughout history, medicinal plants and herbs' use for both dietary purposes and as therapeutic agents have been well documented, and this practice has increased manifold over the past few decades (Woods 1999, Khan et al. 2001). Generally referred to as medicinal plants, these herbs are relied upon by a significant portion of the global population to treat various ailments. Belonging to the Solanaceae or commonly referred to as the nightshade family, *Solanum melongena* (SM), also called the Brinjal, is a vegetable used for culinary purposes that harbors medicinal attributes. In the Ayurvedic system, the use of Brinjal is heavily reported.

Quinic acid, caffeic acid, and other phenolic phytocompounds, such as chlorogenic acid and cinnamic acid, have been discovered in the skin of SM, in recent studies, alongside chemicals including quercetin, nasunin, and a wide array of flavonoids (Helmja et al. 2009, Shen et al. 2005). From the roots, the following compounds have been isolated; isoscopoletin, grossamide, and cannabisin F. A flavonol glycoside, termed, Solanoflavone, has also been extracted from the

white eggplant (Sun et al. 2014, Yoshihara et al. 1978). Antioxidants such as anthocyanin and delphinidin-3-(p-coumaroylrutinoside)-5-glucoside (Nasunin) obtained in high amounts from the peel of the eggplant have inhibited angiogenesis and relieved oxidative stress (Azevedo et al. 2007, Azuma et al. 2008, Jing et al. 2015, Matsubara et al. 2005, Salerno et al. 2014, Noda et al. 2000). Alpha-glucosidase inhibition by the phytochemical, phenylethyl cinnamides, present in the root, is also reported (Liu, Luo, and Kong 2011).

Various anatomical parts of the plant possess anti-inflammatory conditions, cardiotonic, and anti-asthmatic characteristics, as well as have a positive influence on conditions including but not limited to neuropathic pain, nasal ulcers, bacterial infections such as cholera, as well as respiratory diseases of bronchitis and asthma (Warrier et al 1996). Its ability to reduce oxidizing free radicals (Sudheesh et al. 1999, Noda et al. 2000), depress the Central Nervous System (Vohora, Kumar, and Khan 1984), and reduce lipid levels (Sudheesh et al. 1997) has also been discerned.

Various research groups have reported significant hypolipidemic effects in the livers of rats, where a marked decrease in cholesterol, triglyceride, and free fatty acids has been observed upon using the flavonoids obtained from SM fruit (Sudheesh et al. 1997). Cardioprotective effects in preventing ischemic reperfusion injury have been seen when raw or grilled eggplant fruits have been incorporated into the diets of rats (Das et al. 2011). Moreover, in 2001 Lee and colleagues found that water extract of SM decreased mast cell secretion of Tumor Necrosis Factor-alpha (TNF-$\alpha$) and reduced the incidence of cutaneous anaphylactic reactions (Lee et al. 2001). Inflammation caused by the agonists of the protease-activated receptor (PAR 2) was also alleviated upon using the crude aqueous extracts of eggplant fruits. This is achieved by blocking the action myeloperoxidase enzyme and decreasing the production of TNF-$\alpha$ in paw edema in mice (Han et al. 2003)

A global renaissance has occurred regarding using natural products in healthcare. Organizations such as the WHO are stressing the greater importance of scientific inquisition into traditional herbal treatments. Once their clinical value has been determined, many countries of the world are looking to add medicinal plants to the "Essential Drug List" of the WHO. Pakistan and its Northern Regions are rich in medicinal plants (Nasir and Ali 1972). Significant potential exists for the exploration and scientific investigation of novel drug compounds from the indigenous sources of the country. The current research aims to delve into the ability of the crude extract of SM to relieve pain and mitigate inflammation and rationalize its use in traditional medicine in the subcontinent.

## Materials & Methods

### Plant Material

From the market, 5kg of SM was bought. The task of identifying the appropriate variety was given to Dr. Humaira Gul from the Department of Botany of the Faculty of Sciences, University of Karachi. A sample has been kept in the lab for future reference. After being mashed, the fruit pulp, at room temperature, was stored in a tightly closed container.

### Preparation of Plant Extracts

The mashed fruit, for three days with periodic shaking, was soaked in 5 Liters of methanol (70%). Filtration was performed using a Muslin cloth and subsequently a qualitative (20-25 um) Grade 4 Whatman filter paper. The combined filtrate, obtained after three repeats of the filtration process, was placed in a rotatory evaporator and evaporated under reduced pressure to a dark brown, thick, semi-solid mass. The crude extract was generated. The yield of the crude methanolic extract was 18%, with the remaining being the aqueous layer (Aq).

### Animals

Both male and female, 20-30g of NMRI mice and 200-270g of Sprague-Dawley rats were maintained

in the animal facility of the Pak-Austria Fachhchschule: IAST, Pakistan. Using these animal samples for experimental purposes was in compliance with the ethical rules and regulations. The animals had free access to water and food, were exposed to adequate light and dark cycles, and were kept under standard conditions.

**Writhing Test**

As per the method stated by (Koster 1959), male adult mice were used between 6-20 in number. The test was conducted after the random distribution of the animals into three groups: ***Control Group*** (vehicle-treated), ***Standard Group*** administered with the NSAID diclofenac sodium (reference drug), ***Investigational/Test Group*** administered with various doses intraperitoneally injected doses of crude extract (10mg/kg, 20mg/kg and 50mg/kg). The specimens were placed in glass beakers for 5-minute intervals. Prior to placing the mice in the beakers, the mice were injected with the standard drug or crude SM extract for 30 minutes, after which the mice were given a 0.1mL/10g acetic acid formulated as a 0.7% v/v i.p. injection. To ensure standardization of measurement, the term writhe was defined as the abdomen and at least one hind limb stretching together; the number of writhes was counted for a total of 20 minutes. 10mL/kg saline and 10mL/kg diclofenac sodium injected into the peritoneal cavity served as the control and reference drug.

**Formalin Test**

(Hunskaar and Hole 1987) outlined the procedure for performing the formalin-induced pain test. 6-20 mice weighing 20 and 25 grams were separated and grouped as per the fashion mentioned above. 1% formalin in 0.9% Sodium Chloride solution (saline) was prepared up to 20µl and administered into the dorsal hind paw using an injection into the subcutaneous layer. Then the specimens were immediately transferred to a transparent box for observation. In two phases (0-5 minutes) and (15-30 minutes) post formalin injection, the elapsed time of paw licking was gauged. The time for both biting and licking responses was measured in seconds. The animals were subjected to intraperitoneal injections of 10, 20, and 50mg/kg of SM or 10mg/kg i.p. or 5mg/kg i.p. of diclofenac sodium or morphine, depending on the animal group. Extracts or standards were given 30 minutes before the administration of formalin. Before giving the crude extract or morphine, the mice in some groups were injected with 5mg/kg i.p. Naloxone. A vehicle (0.1mL/10g) was given to the Control Group. Percent inhibition of the paw-licking time was calculated, and the results of the animals in the control and experimental groups were compared

**Hot Plate Test**

The hot plate assay, with slight alteration, was performed following the procedural guidelines (Eddy, Leimbach, and Therapeutics 1953). The temperature was 52 ± 0.8°C for the hot plate for this test. Individual Mice weighing 20-25g ($n$ = 6–10) were one by one exposed to the hot plate. The time taken to induce discomfort, i.e., jumping and/or paw licking, was recorded. To prevent any thermal injury to the paws due to the hot plate, the mice were exposed for a maximum of 20 seconds. The animal selection was conducted one day before the test. 50mg/kg plant extract or 5mg/kg morphine intraperitoneal injection was given to the mice half hour before starting the hot plate test. At 30 min, 60 min, 120 min, and 180 min time intervals post-injection of plant extract or morphine, the mice were observed. Naloxone (5mg/kg i.p.) was given 20 minutes before the SM extract or morphine; equal volumes of the vehicle were given to the control group. The latency time was measured in seconds between the control and experimental animals.

**Rat Paw Edema Assay (Anti-inflammatory Activity)**

According to the procedural guidelines and procedural protocols outlined by (Winter, Risley, and Nuss 1962), the carrageenan-induced hind paw edema test was conducted. To remove any bias,

the rats were randomly segregated into categories, with each group consisting of 5-8 animals. The rats were given a 0.05mL subcutaneous injection of carrageenan solution (1%) prepared in distilled (RO) water. Dose of plant extract ranging from 10–50mg/kg i.p. or 20mg/kg diclofenac sodium were introduced i.p., 0.5 hours prior to the carrageenan injection. An equal volume of vehicle was given to the control group. Before and at 60-minute intervals for 4 hours after the carrageenan injection using plethysmomemter Ugo Basile 7150, the edema induced in the paw of the Sprague-Dawley Rats was checked using the volume displacement method. The difference in paw volume, determined before and after injection of the phlogistic agent, indicated the severity of edema.

The % inhibition of the inflammation was determined for each animal by comparison with controls and calculated by the following formula:

$\%I=1-(dt/dc)\times100\%I=1-(dt/dc)\times100$

where "*dt*" is the difference in paw volume in the drug-treated group and "*dc*" the difference in paw volume in control group. "*I*" stands for inhibition.

**Statistical Analysis**

The student *t*-test was used to analyze and compare the control and test group results. The data were presented as Mean ± SEM. One-way analysis of variance (ANOVA) was applied, after which Tukey–Kramer multiple comparison tests were used to analyze the raw data obtained from the hot plate assay. $P < 0.05$ was deemed statistically significant.

**Results**

**Writhing Test**

Pain invoked by acetic acid was significantly alleviated upon the intraperitoneal (i.p.) administration of the methanolic extract of SM at the doses mentioned above ($P < 0.001$), as shown in Table 1. Maximum inhibition of nociception induced by acetic acid was recorded at doses of 50mg/kg at 87%, comparable to that of the diclofenac sodium (standard drug), whereas 60% inhibition was observed at the dose of 20mg/kg i.p.

**Table 1 Effect of the crude methanolic extract of SM and diclofenac sodium on acetic acid-induced writhing in mice.**

| Treatment | Drug | Dose (ip) | Writhing | % Protection |
|---|---|---|---|---|
| Negative Control | Saline | 10mL/kg | 75±8 | |
| Positive Control | Diclofenac Sodium | 20mg/kg | 16±2*** | 79 |
| S. Melongena | Methanolic Extract | 10mg/kg | 30±5*** | 60 |
| | | 20mg/kg | 15±3*** | 80 |
| | | 50mg/kg | 9±2*** | 87 |

**Formalin Test**

Both phases of paw licking caused by formalin were significantly inhibited with P<0.01, P<0.001 upon exposure to the SM extract (10, 20, and 50mg/kg) (Table 2). However, 20mg/kg of Diclofenac Sodium reduced paw licking only in the second phase from 70 ± 5 seconds to 28 ± 4 seconds, producing 60% inhibition. Similarly, in the second phase of the test, the plant extract was able to induce 60, 75, and 84% inhibition of nociception at doses of 10mg/kg, 20mg/kg, and 50mg/kg, respectively (Table 2).

**Table 2 Effect of the methanolic extract of SM and diclofenac sodium on formalin-induced paw-licking time in mice.**

| Treatment Group | Drug | Dose (ip) | Paw-licking time | | % Protection | |
|---|---|---|---|---|---|---|
| | | | 1st phase | 2nd phase | 1st phase | 2nd phase |
| Negative Control | Saline | 10ml/kg | 45±4 | 70±5 | - | - |
| Positive Control | Diclofenac Sodium | 20mg/kg | 43±5 | 28±4** | - | 60 |
| SM | Methanolic Extract | 10mg/kg | 30±6* | 28±5** | 35 | 60 |
| | | 20mg/kg | 15±3** | 17±3*** | 50 | 75 |
| | | 50mg/kg | 9±2** | 11±2*** | 60 | 84 |

**Hot Plate Test**

At the dose of 50mg/kg (i.p.), significant analgesic activity was observed with the SM plant extract, similar to morphine ($P < 0.01$) (Table 3). After being treated with extract, the reaction time of the animals increased from 6.9 ± 0.3 s (control) to 15.1 ± 0.6 s (treated with extract), with the maximum effect attained 2 hours into the test. Naloxone (5mg/kg) pre-treatment neutralized the effect of morphine. Table 3 also delineates that the analgesic effect of the plant extract was partly reversed with naloxone.

**Table 3: Effects of SM and morphine treatments in the presence and absence of naloxone on latency time of mice in hot plate test.**

| Treatment Group | Drug | Dose (ip) | Latency Time (sec) | | | | |
|---|---|---|---|---|---|---|---|
| | | | 0 hr | 0.5 hr | 1 hr | 2 hr | 3 hr |
| Negative Control | Saline | 10ml/kg | 6.5±0.3 | 6.7±0.4 | 6.5±0.4 | 6.9±0.3 | 6.5±0.4 |
| Positive Control | Morphine | 10mg/kg | 6.4±0.4 | 7.9±0.4 | 11.5±0.5*** | 11.8±0.5*** | 11.8±0.4*** |
| Positive Control + Antagonist | Morphine +Naloxone | 10+5 | 5.5±0.3 | 5.7±0.3 | 5.8±0.3 | 5.6±0.4 | 5.6±0.4 |
| SM | Methanolic Extract | 50mg/kg | 7.9±0.4 | 8.1±0.4 | 12.2±0.5*** | 15.1±0.6*** | 14.9±0.6*** |
| SM +Antagonist | Methanolic extract + Naloxone | 50+5 | 6.6±0.3 | 7.1±0.4 | 7.8±0.4 | 9.3±0.5** | 9.2±0.4** |

**Anti-inflammatory Activity**

Localized edema generated from the subplantar carrageenan injection was seen to reach its maximum effect 3 hours post-injection. An increase in the net volume of the rat paw for 4 hours, after which a gradual decline back to normal was the indicator of the presence of local inflammation. Methanolic crude SM extract reduced inflammation at hour three post administration of carrageenan, where at 50mg/kg dose, maximum inhibition of 75% was seen as outlined in Table 4.

**Table 4 Effect of the methanolic extract of SM and diclofenac sodium on carrageenan-induced paw edema in rats.**

| Treatment Group | Drug | Dose (ip) | Initial Paw Volume (ml) | Paw Volume at 3 hr | Increase in Paw Volume | % Protection |
|---|---|---|---|---|---|---|
| Negative Control | Saline | 10ml/kg | 0.80±0.03 | 1.10±0.04 | 0.30 | - |
| Positive Control | Diclofenac Sodium | 20mg/kg | 0.90±0.03 | 1.05±0.03 | 0.15** | 50 |
| SM | Methanolic Extract | 10mg/kg | 0.80±0.04 | 1.01±0.04 | 0.21* | 35 |
| | | 20mg/kg | 0.85±0.03 | 0.99±0.02 | 0.14** | 54 |
| | | 50mg/kg | 0.90±0.02 | 0.98±0.03 | 0.08** | 75 |

The plant extract proved ineffective during the early phase of carrageenan-induced edema. During the third hour of observation, the variation in the paw volume between the investigational and control groups was statistically significant with $P<0.01$. Furthermore, 50% inhibition of the carrageenan-induced edema was seen in the standard group (administered with 20mg/kg i.p. diclofenac sodium) (Table 4). The pharmacological activities of the extract observed in this study are summarized in figure 1.

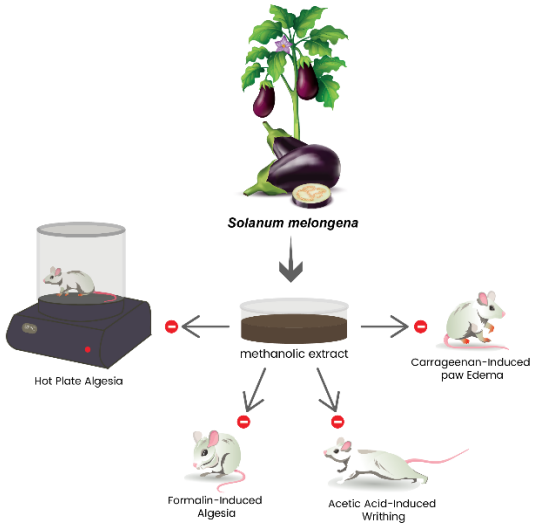


**Figure 1: A summary of the pharmacological activities of SM fruit extract.**

## Discussion

The majority of the third-world populace heavily depends upon traditional remedies from the local flora to treat multiple ailments and pathologies. Out of these countries, Pakistan is a nation that comprises at least 45,000 traditional healers, and most of their practice is concentrated in the rural areas of the country. This figure has remained consistent over the passage of many years. Moreover, 7 out of 10 individuals in these countries rely upon herbal remedies. However, despite the overwhelming application of herbal medicine, herbal remedies are yet to be investigated through a scientific lens, thus reiterating the need for a thorough inquiry into medicinal herbs' pharmacological and therapeutic potential. The lack of technology and conflicts between modern healthcare professionals and traditional healers exacerbates this problem.

In complementary and alternative medicine (CAM), species from multiple botanical families have been used to counter inflammation and pain (Geissler et al. 2002, Dongmo, Nguelefack, and Lacaille-Dubois 2005). Our interest and subsequent study into the anti-inflammatory and analgesic effects of SM have yielded positive results. Widely accepted models such as those mentioned above were employed for antinociceptive studies. For studying the effects of non-central/peripheral analgesics, acetic-acid is used as it can invoke the release in peritoneal fluids of histamine, 5-Hydroxy tryptamine, commonly known as serotonin, and prostaglandins (PGIs) to produce pain (Collier et al. 1968, Deraedt et al. 1980). In this investigation, it was seen that there was similar inhibition by both Diclofenac Sodium and SM of nociception in the acetic acid-induced writhing in mice. Thus, a reasonable hypothesis can be generated that how the plant extract reduces pain might be related to inhibition of the prostaglandin function (Ferreira 1972). Other research groups have combined analgesic drugs, commonly known as pain killers such as aspirin and diclofenac with therapeutic herbs (*Asparagus pubescens* and *Quasia amara*) used in folkloric medicine to manage pain and inflammation (Okpo, Fatokun, and Adeyemi 2001, Nwafor and Okwuasaba 2003, Toma et al. 2003). Their results, have exhibited marked analgesic effects in acetic acid-induced writhing in mice.

However, it cannot be ignored that prostaglandins released by ethanoic acid/acetic acid stimulate both peripheral nociceptors and neurons that can be acted upon by clinically important analgesics such as drugs belonging to the opioid class, NSAIDs, and centrally acting drugs, rendering the acetic acid-induced writhing test in mice a non-selective approach for understanding the analgesic effects of SM (Vaz et al. 1996).

Subsequently, the Formalin test was conducted to unearth the mechanism of pain and analgesia of the crude methanolic extract of SM (Tjølsen et al. 1992). The pain introduced by formalin is biphasic. Phase one pain is because of formalin activation of the sensory neurons. In contrast, the reason for pain in the following phase is the release of pro-inflammatory cytokines such as bradykinin, histamine, 5-HT, and PGIs (Murray, Porreca, and Cowan 1988, Hunskaar and Hole 1987). In our investigation, the reduction in paw licking of mice was similar when the mice were pre-emptively given morphine and different doses of the crude extract. It is documented that NSAIDs only inhibit the late phase in contrast to drugs that act centrally, such as morphine and other opioids that possess the ability to inhibit both phases equally (Santos et al. 1994, Shibata et al. 1989) of nociception caused by formalin. The plant extract's ability to inhibit both phases indicates a centrally acting analgesic mechanism. Opioid receptor activity by the plant extract has also been discerned as the activity of the plant extract was partially inhibited by naloxone, which is clinically used as an antidote against opioids, completely neutralizing the effects of morphine. Henceforth, it is reasonable to conclude that the SM crude extract consists of both NSAID and opioid-like components that in-sync serve to relieve pain as exemplified by the aforementioned animal assays of pain and inflamma-

tion (Christie, Vaughan, and Ingram 1999). Naloxone pre-treatment caused a slight increase in the licking response of the animals in the formalin test, pointing to its antagonistic effect against the endogenous opioid system. *A. ferruginea* and *A. nilotica* (Dhar et al. 1968, Almeida, Navarro, and Barbosa-Filho 2001) among other plants have central analgesic activity, and it is proposed that SM could contain a few comparable constituents with regards to central pain inhibition. The majority of the pain inhibition observed in the second phase is mainly due to the presence of more modes of pain relief, preventing the synthesis of prostaglandins (Tjølsen et al. 1992).

Turner 1965 established that the hot plate assay is a suitable test to investigate central pain inhibition, which was confirmed in our research. Drastically decreased reaction rates that were also partially antagonized by naloxone reinforce the presence of the opioid pharmacological framework in the noticed pain-relieving effect of the SM extract. Reduction in nociception was mainly observed in the second phase of the formalin-induced pain test, similar to that of aspirin and other drugs, for example, phenylbutazone, which can counteract peripheral analgesia (Shibata et al. 1989). It is well known these induce cyclooxygenase enzyme blockade involved in the arachidonic acid pathways for analgesia (Taiwo and Levine 1990). Subsequently, it can be deduced that NSAID-like pain inhibition is seen in the plant extract.

Following the aforementioned findings and the existing use of SM, the carrageenan-induced rat paw edema method was selected to gauge the anti-inflammatory activity of the plant extract. Compared to Diclofenac Sodium (reference drug), SM displayed marked inhibition of inflammation. Two phases govern carrageenan-induced inflammation: Phase one/Early phase, involves edema produced as a result of histamine and serotonin release, and Phase two/Late phase, where relaxing of the walls of the blood vessels, termed vasodilation, is mediated by prostaglandin and bradykinin (Di Rosa, Giroud, and Willoughby 1971, Burch and DeHaas 1990). Many research groups have discerned that the Late phase is susceptible to clinically available anti-inflammatory drugs and is commonly used to study whether natural product extracts harbor anti-phlogistic properties (Della Loggia et al. 1986, Saeed et al. 1995). Our investigation suggests that prostaglandin inhibition is a possible analgesic mechanism of the SM owing to the significant anti-inflammatory effects seen principally in the Late phase of the carrageenan-induced rat paw edema test. The standard drug, Diclofenac sodium, also exhibited a similar anti-edematous effect in the assay. (Skoutakis et al. 1988) showed that Diclofenac Sodium and other NSAIDs inhibit synthesis and prostaglandin production, diminishing arthritic pain, swelling, and inflammation. Cyclooxygenase inhibition is also evidenced regarding chemical constituents that are effective in reducing carrageenan-induced edema (Selvam and Jachak 2004). In light of these findings, it can be stated that the inhibitory activity of the crude extract on the carrageenan-induced inflammation at the third hour is perhaps due to the aforementioned mechanisms.

Thus, it can be safely concluded SM boasts analgesic and anti-inflammatory properties. Our findings suggest that the plant extract functioning is along the lines of that of NSAIDs. Involvement of the opioid system is also inferred due to naloxone's partial analgesic reversal of the SM extract. The data currently available strongly indicate that SM bears demonstrate significant potential as a source of novel analgesic compounds. It is possible that terpenoids and flavonoids in the plant extract may be possible to reduce pain and inflammation as plant sources containing such phytochemicals in excess tend to show positive results in inflammation and pain assays (Della Loggia et al. 1986, Saeed et al. 2010). Our data, to some extent, justify the anti-inflammatory and analgesic use of SM. However, deeper and more extensive studies are required to identify the phytochemicals involved and their exact mechanisms of the reported effects of the plant extract.

**Conflict of Interest**

The authors declare that they have no competing interests.

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**Study Approval**

Yes. The Institutional Review Board & Ethics Committee of the Kohat University of Science & Technology approved the study.

**Consent Forms**

NA.

**Authors Contribution**

SJ and MIK conceptualized the study and wrote the final manuscript; BA, VN, JK did the experiments and, collected the data, and helped in writing the first draft; MIK supervised the whole project and wrote the final manuscript.

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**References**

Almeida, RN, DS Navarro, and JM %J Phytomedicine Barbosa-Filho. 2001. "Plants with central analgesic activity." 8 (4):310-322.

Azevedo, Luciana, Patrícia L Alves de Lima, José C Gomes, Paulo C Stringheta, Daniel A Ribeiro, Daisy MF %J Food Salvadori, and Chemical Toxicology. 2007. "Differential response related to genotoxicity between eggplant (Solanum melanogena) skin aqueous extract and its main purified anthocyanin (delphinidin) in vivo." 45 (5):852-858.

Azuma, Keiko, Akio Ohyama, Katsunari Ippoushi, Takashi Ichiyanagi, Atsuko Takeuchi, Takeo Saito, Hiroyuki %J Journal of agricultural Fukuoka, and food chemistry. 2008. "Structures and antioxidant activity of anthocyanins in many accessions of eggplant and its related species." 56 (21):10154-10159.

Burch, Ronald M, and Christopher %J Naunyn-Schmiedeberg's archives of pharmacology DeHaas. 1990. "A bradykinin antagonist inhibits carrageenan edema in rats." 342 (2):189-193.

Christie, MJ, CW Vaughan, and SL %J Inflammation Research Ingram. 1999. "Opioids, NSAIDs and 5-lipoxygenase inhibitors act synergistically in brain via arachidonic acid metabolism." 48 (1):1-4.

Collier, HO, LC Dinneen, Christine A Johnson, C1 %J British journal of pharmacology Schneider, and chemotherapy. 1968. "The abdominal constriction response and its suppression by analgesic drugs in the mouse." 32 (2):295.

Das, S, U Raychaudhuri, M Falchi, A Bertelli, PC Braga, Dipak K %J Food Das, and function. 2011. "Cardioprotective properties of raw and cooked eggplant (Solanum melongena L)." 2 (7):395-399.

Della Loggia, Roberto, Aurelia Tubaro, P Dri, C Zilli, P %J Progress in clinical Del Negro, and biological research. 1986. "The role of flavonoids in the anti-inflammatory activity of Chamomilla recutita." 213:481-484.

Deraedt, Roger, Simone Jouquey, Françoise Delevallée, and Micheline %J European journal of pharmacology Flahaut. 1980. "Release of prostaglandins E and F in an algogenic reaction and its inhibition." 61 (1):17-24.

Dhar, M. L., M. M. Dhar, B. N. Dhawan, B. N. Mehrotra, and C. Ray. 1968. "Screening of Indian plants for biological activity: I." *Indian J Exp Biol* 6 (4):232-47.

Di Rosa, ML, JP Giroud, and DA %J The Journal of pathology Willoughby. 1971. "Studies of the mediators of the acute inflammatory response induced in rats in different sites by carrageenan and turpentine." 104 (1):15-29.

Dongmo, AB, T Nguelefack, and MA %J Journal of ethnopharmacology Lacaille-Dubois. 2005. "Antinociceptive and anti-inflammatory activities of Acacia pennata wild (Mimosaceae)." 98 (1-2):201-206.

Eddy, Nathan B, Dorothy %J Journal of Pharmacology Leimbach, and Experimental Therapeutics. 1953. "Synthetic analgesics. II. Dithienylbutenyl-and dithienylbutylamines." 107 (3):385-393.

Ferreira, SH %J Nature New Biology. 1972. "Prostaglandins, aspirin-like drugs and analgesia." 240 (102):200-203.

Geissler, P Wenzel, Stephen A Harris, Ruth J Prince, Anja Olsen, R Achieng'Odhiambo, Helen Oketch-Rabah, Philister A Madiega, Anne Andersen, and Per %J Journal of Ethnopharmacology Mølgaard. 2002. "Medicinal plants used by Luo mothers and children in Bondo district, Kenya." 83 (1-2):39-54.

Han, S. W., J. Tae, J. A. Kim, D. K. Kim, G. S. Seo, K. J. Yun, S. C. Choi, T. H. Kim, Y. H. Nah, and Y. M. Lee. 2003. "The aqueous extract of Solanum melongena inhibits PAR2 agonist-induced inflammation." *Clin Chim Acta* 328 (1-2):39-44. doi: 10.1016/s0009-8981(02)00377-7.

Helmja, Kati, Merike Vaher, Tõnu Püssa, and Mihkel %J Journal of Chromatography A Kaljurand. 2009. "Analysis of the stable free radical scavenging capability of artificial polyphenol mixtures and plant extracts by capillary electrophoresis and liquid chromatography–diode array detection–tandem mass spectrometry." 1216 (12):2417-2423.

Hunskaar, Steinar, and Kjell %J Pain Hole. 1987. "The formalin test in mice: dissociation between inflammatory and non-inflammatory pain." 30 (1):103-114.

Jing, Pu, Bingjun Qian, Shujuan Zhao, Xin Qi, Ludan Ye, M Mónica Giusti, and Xingya %J Food chemistry Wang. 2015. "Effect of glycosylation patterns of Chinese eggplant anthocyanins and other derivatives on antioxidant effectiveness in human colon cell lines." 172:183-189.

Khan, I. A., J. Allgood, L. A. Walker, E. A. Abourashed, D. Schlenk, and W. H. Benson. 2001. "Determination of heavy metals and pesticides in ginseng products." *J AOAC Int* 84 (3):936-9.

Koster, R. 1959. "Acetic acid for analgesic screening." Fed proc.

Lee, Young-Mi, Hyun-Ja Jeong, Ho-Jeong Na, Ji-Yeon Ku, Dae-Ki Kim, Goo Moon, Han-Jung Chae, Hyung-Ryong Kim, Seung-Hwa Baek, and Hyung-Min %J Pharmacological Research Kim. 2001. "Inhibition of immunologic and nonimmunologic stimulation-mediated anaphylactic reactions by water extract of white eggplant (Solanum melongena)." 43 (4):405-409.

Liu, X., J. Luo, and L. Kong. 2011. "Phenylethyl cinnamides as potential alpha-glucosidase inhibitors from the roots of Solanum melongena." *Nat Prod Commun* 6 (6):851-3.

Matsubara, Kiminori, Takao Kaneyuki, Tsuyoshi Miyake, Masaharu %J Journal of agricultural Mori, and food chemistry. 2005. "Antiangiogenic activity of nasunin, an antioxidant anthocyanin, in eggplant peels." 53 (16):6272-6275.

Murray, Christopher W, Frank Porreca, and Alan %J Journal of pharmacological methods Cowan. 1988. "Methodological refinements to the mouse paw formalin test: an animal model of tonic pain." 20 (2):175-186.

E. Nasir and S. I. Ali, "Flora of Pakistan," National Herbarium, NARC, Islamabad, Department of Botany, University of Karachi, Karachi, (Fascicles), 1972-1994.

Noda, Y., T. Kneyuki, K. Igarashi, A. Mori, and L. Packer. 2000. "Antioxidant activity of nasunin, an anthocyanin in eggplant peels." *Toxicology* 148 (2-3):119-23. doi: 10.1016/s0300-483x(00)00202-x.

Nwafor, P. A., and F. K. Okwuasaba. 2003. "Antinociceptive and anti-inflammatory effects of methanolic extract of Asparagus pubescens root in rodents." *J Ethnopharmacol* 84 (2-3):125-9. doi: 10.1016/s0378-8741(02)00213-1.

Okpo, S. O., F. Fatokun, and O. O. Adeyemi. 2001. "Analgesic and anti-inflammatory activity of Crinum glaucum aqueous extract." *J Ethnopharmacol* 78 (2-3):207-11. doi: 10.1016/s0378-8741(01)00318-x.

Saeed, M. K., Y. Deng, R. Dai, W. Li, Y. Yu, and Z. Iqbal. 2010. "Appraisal of antinociceptive and anti-inflammatory potential of extract and fractions from the leaves of Torreya grandis Fort Ex. Lindl."

*J Ethnopharmacol* 127 (2):414-8. doi: 10.1016/j.jep.2009.10.024.

Saeed, S. A., R. U. Simjee, G. Shamim, and A. H. Gilani. 1995. "Eugenol: a dual inhibitor of platelet-activating factor and arachidonic acid metabolism." *Phytomedicine* 2 (1):23-8. doi: 10.1016/s0944-7113(11)80044-9.

Salerno, L., M. N. Modica, V. Pittalà, G. Romeo, M. A. Siracusa, C. Di Giacomo, V. Sorrenti, and R. Acquaviva. 2014. "Antioxidant activity and phenolic content of microwave-assisted Solanum melongena extracts." *ScientificWorldJournal* 2014:719486. doi: 10.1155/2014/719486.

Santos, A. R., V. C. Filho, R. Niero, A. M. Viana, F. N. Moreno, M. M. Campos, R. A. Yunes, and J. B. Calixto. 1994. "Analgesic effects of callus culture extracts from selected species of Phyllanthus in mice." *J Pharm Pharmacol* 46 (9):755-9. doi: 10.1111/j.2042-7158.1994.tb03897.x.

Selvam, C., and S. M. Jachak. 2004. "A cyclooxygenase (COX) inhibitory biflavonoid from the seeds of Semecarpus anacardium." *J Ethnopharmacol* 95 (2-3):209-12. doi: 10.1016/j.jep.2004.07.026.

Shen, G., P. Van Kiem, X. F. Cai, G. Li, N. T. Dat, Y. A. Choi, Y. M. Lee, Y. K. Park, and Y. H. Kim. 2005. "Solanoflavone, a new biflavonol glycoside from Solanum melongena: seeking for anti-inflammatory components." *Arch Pharm Res* 28 (6):657-9. doi: 10.1007/bf02969354.

Shibata, Manabu, Tsuyako Ohkubo, Hiroshi Takahashi, and Reizo %J pain Inoki. 1989. "Modified formalin test: characteristic biphasic pain response." 38 (3):347-352.

Skoutakis, V. A., C. A. Carter, T. R. Mickle, V. H. Smith, C. R. Arkin, J. Alissandratos, and D. E. Petty. 1988. "Review of diclofenac and evaluation of its place in therapy as a nonsteroidal anti-inflammatory agent." *Drug Intell Clin Pharm* 22 (11):850-9. doi: 10.1177/106002808802201102.

Sudheesh, S., G. Presannakumar, S. Vijayakumar, and N. R. Vijayalakshmi. 1997. "Hypolipidemic effect of flavonoids from Solanum melongena." *Plant Foods Hum Nutr* 51 (4):321-30. doi: 10.1023/a:1007965927434.

Sudheesh, S., C. Sandhya, A. Sarah Koshy, and N. R. Vijayalakshmi. 1999. "Antioxidant activity of flavonoids from Solanum melongena." *Phytother Res* 13 (5):393-6. doi: 10.1002/(sici)1099-1573(199908/09)13:5<393::aid-ptr474>3.0.co;2-8.

Sun, J., Y. F. Gu, X. Q. Su, M. M. Li, H. X. Huo, J. Zhang, K. W. Zeng, Q. Zhang, Y. F. Zhao, J. Li, and P. F. Tu. 2014. "Anti-inflammatory lignanamides from the roots of Solanum melongena L." *Fitoterapia* 98:110-6. doi: 10.1016/j.fitote.2014.07.012.

Taiwo, Y. O., and J. D. Levine. 1990. "Effects of cyclooxygenase products of arachidonic acid metabolism on cutaneous nociceptive threshold in the rat." *Brain Res* 537 (1-2):372-4. doi: 10.1016/0006-8993(90)90389-s.

Tjølsen, A., O. G. Berge, S. Hunskaar, J. H. Rosland, and K. Hole. 1992. "The formalin test: an evaluation of the method." *Pain* 51 (1):5-17. doi: 10.1016/0304-3959(92)90003-t.

Toma, W., J. S. Gracioso, C. A. Hiruma-Lima, F. D. Andrade, W. Vilegas, and A. R. Souza Brito. 2003. "Evaluation of the analgesic and antiedematogenic activities of Quassia amara bark extract." *J Ethnopharmacol* 85 (1):19-23. doi: 10.1016/s0378-8741(02)00334-3.

Turner RA (1965) Screening methods in pharmacology, vol 1. Academic Press, New York, pp 85–106.

Vaz, Z. R., V. C. Filho, R. A. Yunes, and J. B. Calixto. 1996. "Antinociceptive action of 2-(4-bromobenzoyl)-3-methyl-4,6-dimethoxy benzofuran, a novel xanthoxyline derivative on chemical and thermal models of nociception in mice." *J Pharmacol Exp Ther* 278 (1):304-12.

Vohora, S. B., I. Kumar, and M. S. Khan. 1984. "Effect of alkaloids of Solanum melongena on the central nervous system." *J Ethnopharmacol* 11 (3):331-6. doi: 10.1016/0378-8741(84)90078-3.

Warrier PK, Nambiar VPK, Rammanakutty C, (1996). Indian Medicinal. Plants. Madras (India): a compendium of 500 species by Orient Longman, Limited, Published by Orient Blackswan, ISBN 8125007636, 9788125007630, 57.

Winter, C. A., E. A. Risley, and G. W. Nuss. 1962. "Carrageenin-induced edema in hind paw of the rat as an assay for antiiflammatory drugs." *Proc Soc Exp Biol Med* 111:544-7. doi: 10.3181/00379727-111-27849.
Woods, PW %J Essence. 1999. "Herbal healing." 30 (3):42-4.
Yoshihara, Teruhiko, Seiji Takamatsu, Sadao %J Agricultural Sakamura, and Biological Chemistry. 1978. "Three new phenolic amides from the roots of eggplant (Solanum melongena L.)." 42 (3):623-627.