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ANALGESIC ACTIVITY OF ETHANOLIC, HEXANE AND CHLOROFORM EXTRACTS OF SESAME SEED BY THERMAL HEAT METHOD IN ALBINO MICE

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ABSTRACT: Background: Pain is a common symptom having huge public health importance. Conventional analgesics relieve pain effectively but cause various unwanted side effects. Hence the search for a novel analgesic with favourable risk-benefit profile is essential. **Objectives:** The current study was undertaken to investigate the analgesic activity of the ethanolic, hexane and chloroform extracts of sesame seeds by thermal heat method in Albino mice. **Methods:** The mice were divided into 5 groups. Group 1 was administered normal saline. Group 2 was given aspirin (50 mg/kg). Groups 3 to 5 were administered the various Sesame seed extracts (ethanolic, hexane and chloroform) at the doses of 100, 150 and 200 mg/kg, respectively. All drugs were administered orally. Analgesic activity was evaluated by hot plate method. **Results:** The ethanolic extract of Sesame seed at the dose of 100 mg/kg and 150 mg/kg exhibited significant analgesic activity at 120 and 180 minutes, whereas at a dose of 200 mg/kg it exhibited activity even at 60 minutes. The maximum analgesic effect was shown at 120 minutes. The activity of extract at 200 mg/kg was comparable to aspirin. Both the hexane and chloroform extract of Sesame seed did not exhibit significant analgesic effect at a dose of 100 mg/kg and 150 mg/kg. But at a higher dose (200 mg/kg), both hexane and chloroform extract showed significant analgesic activity, which was maximum at 180 minutes. **Conclusion:** The ethanolic, hexane, and chloroform extracts of Sesame seeds have analgesic potential. The analgesic activity of the ethanolic extract is comparable to aspirin.

INTRODUCTION: Algesia or pain is a sensory and emotional experience that is unpleasant and related to tissue damage, actual or potential. It is usually a warning signal. It is predominantly protective in nature but frequently causes distress and adverse consequences [1-3].

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Globally, the burden of morbidity due to pain is enormous. It has been estimated that 20% of adults and 15%–25% of children and adolescents suffer from pain [4]. The cumulative cost of health care related to pain has been higher than that of cancer, heart disease, or diabetes [5].

Hence, the pain has a serious impact on public health. Pain management should be effective and safe. For decades, conventional analgesics, non-steroidal anti-inflammatory drugs (NSAIDs) and opioids have been used for effective pain management. However, their use is associated with side effects ranging from gastrointestinal and renal

to addiction, dependence and respiratory depression [6-9]. Therefore, there is a need to discover novel analgesics that can be used as alternative to conventional drugs. Natural products have a crucial role in modern drug development. The compounds derived from plants have been used with better patient tolerance for a long time and are well accepted [10]. Sesame (*Sesasum indicum Linn*) is a medicinal plant that belongs to the Pedaliaceae family [11]. Sesame seeds are rich in biologically active phytochemicals such as lignans (sesamin, sesamolin, sesaminol and sesamolinol), tocopherols, PUFA, phytosterols, phytates, and other phenolics which contribute to its pharmacological properties [12]. It is reported to possess antiproliferative, neuroprotective, anti-cholesterol, antihypertensive, anti-inflammatory properties [13-19]. Sesame seed consumption is reported to enhance plasma γ-tocopherol and vitamin E activity and prevent cancer and heart diseases [20].

The present study was conducted to search for a novel analgesic with favourable benefit-risk profile. The analgesic potential of three extracts of sesame seeds (ethanolic, hexane, and chloroform) was investigated by thermal heat model (hot plate method) in Albino mice.

METHODS:

Chemicals: The standard drug - aspirin, was procured from Daburpharma Ltd, Tarapur, Thane. Ethanol and other chemicals were purchased from Sigma Aldrich Pvt Ltd, Bengaluru, India. All chemicals were of analytical grade.

Preparation of Plant Extract: The sun-dried Sesame seeds were powdered in a mortar. The dry powder was taken in the Soxhlet apparatus, and extraction was done using different solvents like ethanol, n-hexane and chloroform. A rotary evaporator was used to concentrate the filtrate. After extraction excess solvent was distilled at 80°C. The extract so obtained was stored in sterile bottles.

Animals: Albino mice weighing 30-40 g were used. They were procured from the central animal house, Sri Kaliswari College, Sivakasi, India. They were kept at 12 h: 12 h light-dark cycle. Standard pellets and water were provided *ad libitum*. 12 hours before drug administration, food was withdrawn and reinstituted only after the completion of the experiment. Institutional Animal Ethical Committee approved (PIMSRC/E1/388A/42/2015) the study protocol.

Experiment: The animals were divided into 5 groups. Group 1 was given normal saline (0.1 ml/kg) and served as control. Group 2 was administered the standard drug - Aspirin (50 mg/kg). The test groups (Groups 3 to 5) were administered the various Sesame seed extracts (ethanolic, hexane, and chloroform) at 100, 150, and 200 mg/kg, respectively. All drugs were administered by oral route. Analgesic activity was evaluated by the hot plate method.

Hot Plate Method: The test was performed as per the modified method of Eddy and Leimbach [21]. Mice were placed on a hot plate maintained at 55°C within a restrainer. The cut-off time was 10 seconds to prevent thermal injury to the paws. The time taken by the mice to react to the thermal stimuli, either by licking their paw or jumping, was recorded as the latency period. The latency period was recorded before and at various intervals after administration of the respective treatments (30, 60, 120, and 180 min). A compound with analgesic activity increases the latency period.

Statistical Analysis: The data was stated as mean ± standard error of mean (SEM). One-way ANOVA and Dunnets test analyzed the data as post hoc. *P-value* < 0.05 was considered significant.

RESULTS:

Analgesic Effect of Ethanolic Extract of Sesame Seed: The analgesic effect results of Sesame ethanolic extract are summarised in (**Table 1)**. There was no significant difference in the latency period among the different groups at 0 minute. The latency period of the control group (Group 1) did not vary significantly throughout the observation period. Group 2 which was administered Aspirin (50 mg/kg) (Standard) exhibited significant difference in the latency period at 60 ($p < 0.05$), 120 and 180 minutes ($P < 0.01$). The maximum effect is seen at 180 minutes. The administration of the ethanolic extract at 100 mg/kg and 150 mg/kg (Group 3 and 4, respectively) showed significant analgesic activity only at 120 and 180 minutes (p <

0.05). Group 5 which was administered ethanolic extract (200 mg/kg) exhibited significant analgesic activity at 60 (p< 0.05), 120 and 180 min (p < 0.01). The maximum effect of the extract at all doses was seen at 120 min. The ethanolic extract at 200 mg/kg (Group 5) exhibited an analgesic effect comparable to the standard drug, Aspirin (Group 2) **Table 1.**

TABLE 1: ANALGESIC EFFECT OF ETHANOLIC EXTRACT OF SESAME SEED

Treatment group	Treatment given	Latency period in seconds				
		0 min	30 min	60 min	120 min	180 min
Group 1	Normal saline (0.1 ml/kg)	1.4 ±0.05	1.4 ±0.07	1.5 ±0.01	1.52± 0.08	1.6± 0.02
Group 2	Aspirin (50 mg/kg)	1.38 ±0.07	1.9 ± 0.02	4.6± 0.08*	5.4 ± 0.07**	5.9 ± 0.03**
Group 3	Sesame seed extract (100 mg/kg)	1.39 ±0.04	2.0 ± 1.02	2.2 ± 0.05	4.7± 0.02*	4.6 ± 0.06*
Group 4	Sesame seed extract (150 mg/kg)	1.4 ±0.06	2.3± 0.09	2.6± 0.03	4.9± 1.02*	4.8± 0.07*
Group 5	Sesame seed extract (200 mg/kg)	1.4 ±0.04	3.2 ± 0.06	4.2± 0.04*	5.1± 0.11**	5.0± 0.13**

Data is presented as mean ± SEM. *=P < 0.05, **=P < 0.01 compared with control.

Analgesic Effect of Hexane Extract of Sesame Seed: The results of analgesic activity of Sesame hexane extract are summarised in **Table 2**.

The latency period of all experimental groups was comparable during the pretreatment period. Aspirin administration at 50 mg/kg (Group 2) increased the latency period significantly at 60, 120 and 180 minutes (p < 0.01). Compared to the control group, Group 3 and 4 which were administered Sesame hexane extract at the dose of 100 mg/kg and 150 mg/kg, respectively, did not significantly increase latency.

However, at the dose of 200 mg/kg, Sesame hexane extract (Group 5) showed a significant analgesic effect from 60 minutes onwards (p< 0.05). The maximum analgesic effect of both aspirin and hexane extract at 200 mg/kg (Group 5) was observed at 180 min **(Table 2).**

TABLE 2: ANALGESIC EFFECT OF HEXANE EXTRACT OF SESAME SEED

Treatment group	Treatment given	Latency period in seconds				
		0 min	30 min	60 min	120 min	180 min
Group 1	Normal saline (0.1 ml/kg)	1.39 ±0.07	1.39 ±0.09	1.36 ±0.08	1.33± 0.05	1.36± 0.01
Group 2	Aspirin (50 mg/kg)	1.4 ±0.01	1.8 ± 0.02	4.8± 0.08**	5.5± 0.02**	5.8± 0.07**
Group 3	Sesame seed extract (100 mg/kg)	1.39 ±0.03	1.7 ± 1.0	2.8 ± 0.09	2.9 ± 0.03	2.9 ± 0.05
Group 4	Sesame seed extract (150 mg/kg)	1.39 ±0.02	1.8± 0.14	2.9± 0.47	3.3± 0.49	3.1± 0.47
Group 5	Sesame seed extract (200 mg/kg)	1.4 ±0.04	2.4 ± 1.03	3.8± 0.06*	3.9± 0.05*	4.1± 0.12*

Data is presented as mean ± SEM. *=P < 0.05, **=P < 0.01compared with control.

Analgesic Effect of Chloroform Extract of Sesame Seed: The results of analgesic activity of Sesame chloroform extract are summarised in **Table 3**.

There was no significant difference in the latency periods of different groups at baseline. Group 2 (Aspirin 50 mg/kg) exhibited a significant analgesic effect from 60 minutes till the end of the observation period (p< 0.01). There was no significant increase in latency period in Groups 3 and 4 which were administered Sesame chloroform extract at the dose of 100 mg/kg and 150 mg/kg, respectively.

In contrast to this, Group 5 (Sesame chloroform extract at 200 mg/kg) exhibited a significant analgesic activity as compared to the control (p < 0.05). Both aspirin and chloroform extract at a dose of 200 mg/kg (Group 5) exhibited a maximum effect of 180 min **(Table 3).**

TABLE 3: ANALGESIC EFFECT OF CHLOROFORM EXTRACT OF SESAME SEED

Treatment group	Treatment given	Latency period in seconds				
		0 min	30 min	60 min	120 min	180 min
Group 1	Normal saline (0.1 ml/kg)	1.4 ±0.01	1.41 ±0.04	1.47 ±0.05	1.51± 0.09	1.45± 0.04
Group 2	Aspirin (50 mg/kg)	1.4 ±0.05	1.8± 0.08	4.7± 0.02**	5.3± 0.03**	5.8± 0.01**
Group 3	Sesame seed extract (100 mg/kg)	1.4 ±0.03	1.9 ± 0.13	2.0 ± 0.05	2.19 ± 0.10	2.8 ± 0.06
Group 4	Sesame seed extract (150 mg/kg)	1.39 ±0.02	2.0± 0.01	2.1± 0.11	2.2± 0.04	2.9± 0.17
Group 5	Sesame seed extract (200 mg/kg)	1.38 ±0.06	2.3 ± 0.10	3.9± 0.02*	4.0± 0.03*	4.5± 0.06*

Data is presented as mean ± SEM. *=P < 0.05, **=P < 0.01 compared with control.

DISCUSSION: The present study was conducted to evaluate the analgesic potential of Sesame seed extracts namelyethanolic hexane and chloroform extracts, by hot plate method in albino mice. The hot plate method is a pain model using thermal stimuli to evaluate compounds having central analgesic activity [22]. It is an acute pain model and induces pain by thermal damage to tissues and inflammation and release of peripheral mediators [23, 24]. The pain reflex behaviour exhibited by the experimental animals to the thermal stimuli, namely paw licking or jumping are supraspinally integrated. The paw licking behaviour can be modified only by opioids but the jumping behaviour can be modified even by NSAIDs [25]. Because of the similarities in anatomy and physiology between the two species, murine models can be used to test drugs for human use. Despite the poor face and construct validity, this model can be used for predicting the efficacy of opioid analgesics in humans [26, 27].

In the current study, the ethanolic extract of a Sesame seed at the dose of 100 mg/kg and 150 mg/kg exhibited significant analgesic activity at 120 and 180 min, whereas at a dose of 200 mg/kg, it exhibited activity even at 60 min. The maximum analgesic effect was shown at 120 minutes. The activity of extract at 200 mg/kg was comparable to aspirin, the standard drug in this study. Both the hexane and chloroform extract of Sesame seed did not exhibit significant analgesic effect at 100 mg/kg and 150 mg/kg. But at a higher dose (200 mg/kg), both hexane and chloroform extract showed significant analgesic activity, which was maximum at 180 min. Aspirin exhibited maximum effect at 180 min. This indicates that the ethanolic extract of Sesame seed has a quicker onset of action, whereas hexane and chloroform extract of Sesame seed have similar onset of action as aspirin in this study. The findings of our study are consistent with other studies that reported the analgesic activity of sesame in thermal pain models [28, 29]. Other pain models also reported the analgesic activity of ethanolic extract of sesame seeds [30].

Sesame seeds contain sesamin, a lignan and polyunsaturated fatty acids that may be responsible for their pharmacological activities.[31] The activity of sesamin and fatty acids in thermal pain models is widely reported [32,33].

It is also reported that pretreatment with naloxone also blocked the analgesic activity of sesamin [29]. These reports, taken, together with the results of our study, indicate that the analgesic activity of Sesame could involve opiate-like mechanisms. However, further studies are required to elucidate the exact mechanism of analgesic activity of Sesame.

CONCLUSION: The ethanolic, hexane, and chloroform extracts of Sesame seeds have analgesic effect in albino mice in the thermal pain model. The analgesic effect of ethanolic extract of Sesame seeds is comparable to aspirin, the standard drug in the current study. The analgesic activity may involve a supraspinal mechanism similar to opiates and is attributed to sesamin and polyunsaturated fatty acids abundant in Sesame seeds. However, further studies are required to confirm the extract analgesic mechanism.

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Declarations:

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CONFLICTS OF INTEREST: none declared

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