ORIGINAL ARTICLE

Pharmacological effects of methanolic extract of *Swietenia mahagoni* Jacq (meliaceae) seeds

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Seeds of medicinal plants are common ingredients of many folk and herbal medicines, and seed extracts have been reported to possess pharmacological activity including anti-inflammatory activity. In the present investigation, the methanolic extract of the dried ground seeds of *Swietenia mahagoni* (SMSE) has been evaluated for anti-inflammatory, analgesic, and antipyretic activities. The anti-inflammatory activity was evaluated using acute, sub-chronic, and chronic models of inflammation in rodents. The antipyretic and analgesic activities were evaluated in mice models. Acute toxicity studies revealed that the extract up to a dose of 1.2 g/kg intraperitoneally was nontoxic. SMSE at doses of 50 and 100 mg/kg, i.p. was found to possess anti-inflammatory, analgesic, and antipyretic activities and the effect was comparable with that produced by the standard drug, ibuprofen. The results of the experiment on arachidonic acid-induced paw edema in rat revealed that the extract produces anti-inflammatory activity through dual inhibition of the cyclo-oxygenase and lipo-oxygenase pathways of arachidonic acid metabolism. SMSE also enhanced peritoneal cell exudates along with macrophage significantly. The triterpenoids present in SMSE may be responsible for these activities. SMSE possesses anti-inflammatory, analgesic, and antipyretic activities.

Key words: *Swietenia mahagoni* seed, triterpenoids, anti-inflammatory, analgesic, antipyretic effects

INTRODUCTION

Seeds of medicinal plants are common ingredients of many folk and herbal medicines,[1-3] and seed extracts have been reported to possess pharmacological activity including anti-inflammatory activity.[4-7] *Swietenia mahagoni* Jacq (*Meliaceae*) is a large evergreen tree of immense oriental value. Not much work has been done with the seeds of this plant. The work carried out with the seed extract so far has revealed that it contains triterpenoids possessing anti-platelet activity and limonoids possessing anti-microbial activity.[8,9] Since the plant belongs to the same *meliaceae* family as neem (*azadirachta indica*), it is expected that it might also be a storehouse of many chemicals of medicinal and pharmacological interest. In the present investigation, the methanolic extract of the dried ground seeds has been evaluated for anti-inflammatory, analgesic, and antipyretic activities.

MATERIALS AND METHODS

Plant Materials

The seeds of *S. mahagoni* were collected by a local supplier from in and around Kolkata, India, in 2003. The plant was identified by Botanical survey of India, Sibpur, Howrah, India, where a voucher specimen is kept (SG 001). The fresh seeds were supplied on the day of collection in polybags.

Extraction and Preparation of Test Samples

One kg of *S. mahagoni* seeds was sun dried, ground in a laboratory grinder, and soxhleted for 72 hours in petroleum ether at 20–30°C. Petroleum ether was evaporated by a rotary evaporator to get 69 g of pale yellow liquid with precipitate of a white colored amorphous compound. The residue was dried and again soxhleted for 48 hours in methanol at 70°C. Methanol was evaporated to obtain a dark brown powder (10 g) that was kept in a dessicator at 4°C. This material was designated as SMSE (*S. mahagoni* seed extract) and was dissolved in distilled water to make a stock solution that was prepared fresh before the animal experiments were carried out.

Animals

Experiments were carried out on albino rats (Sprague–Dawley strain) weighing 125–150 g and Balb-C mice weighing 20–25g bred in the Institute's animal house. The animals were housed under conditions of 24 ± 2°C, 50 ± 5% humidity and 12 hours light and 12 hours dark cycle. During maintenance, the animals received a diet of food pellets (fortified with minerals and vitamins) prepared in

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the animal house and water ad libitum. All animal studies were carried out after getting clearance from Institute Animal Ethics Committee (IAEC).

Chemicals

Acetyl salicylic acid, arachidonic acid, carrageenan, croton oil, ibuprofen, indomethacin, and Freund's complete adjuvant were purchased from Sigma; acetic acid from M/S E. Merck and BW 755C was a gift from Burrows Welcome and all other chemicals were of analytical grade purchased locally.

Acute Toxicity Studies

Mice were divided into groups of 10 and SMSE was injected i.p in increasing doses. The LD_{50} (24 hours) was calculated according to Ghosh.[10]

Anti-inflammatory Studies

Carrageenan-induced edema

The rats were divided into four groups (n = 6) and the first group served as the control and received normal saline (0.1 ml/100 g i.p.) The second group was administered with ibuprofen (100 mg/kg i.p.) as the standard reference drug. Groups 3 and 4 received 50 mg and 100 mg/kg i.p. SMSE, respectively. Edema was produced by the method described by Winter *et al*.[11] Carrageenan (0.1 ml/100 g from a 10 mg/ml solution) was injected into the plantar aponeurosis of right hind paw of the rats of all the groups 30 minutes later. The left hind paw served as the control. The paw volume was measured after 4 hours using a plethysmometer (UGO BASILE).

Cotton pellet-induced granuloma

Two autoclaved cotton pellets weighing 10 ± 1 mg were implanted subcutaneously into both sides of the groin region of each rat.[12] The animals were divided into four groups containing six animals in each group. Group I served as control and received normal saline daily at a dose of 0.1 ml/100 g i.p. body weight, group II received ibuprofen (standard drug) daily at a dose of 100 mg/kg i.p. and groups III and IV received SMSE at doses of 50 mg and 100 mg/kg i.p., respectively, for seven consecutive days. After 7 days the animals were sacrificed by cervical dislocation and the pellets together with the granuloma tissues were carefully dissected, dried in an oven at 60°C weighed and compared with control.[12]

Croton oil-induced ear inflammation

Croton oil irritant solution (0.1 ml) prepared according to Brooks *et al*.[13] was applied to the inner surface of the right ear of mice. The mice were divided into four groups of six animals in each group. While mice of group I (control) received 0.1 ml/10 g of normal saline i.p, those of group II received 100 mg/kg i.p. ibuprofen (standard drug) and mice of groups III and IV were administered with 50 mg and 100 mg/kg i.p of SMSE, respectively, 30 minutes before croton oil application. The mice were sacrificed by cervical dislocation after 4 hours, and 7 mm punches were made in the ear by a cork borer. Each ear disc was weighed and compared with control.

Freund's adjuvant-induced polyarthritis

The method of Newbould[14] was followed. Twenty-four male albino rats were divided into four groups of six animals in each group. On day 1, 0.1 ml of Freund's complete adjuvant was injected into the plantar pad of each rat. While rats of group I (control) received 0.1ml/100g of normal saline i.p, those of group II received 100 mg/kg i.p. ibuprofen and groups III and IV received 50 mg and 100 mg/kg SMSE i.p., respectively, for twenty-one consecutive days. The paw volume for each group was measured using plethysmometer (UGO BASILE) on day 0 before administration of adjuvant and on day 21 after treatment and the percentage inhibition was calculated. Severity and development of secondary lesions were also compared.

Arachidonic acid-induced paw edema

The rats were divided into five groups of six animals in each group. Group I served as control and received 0.1 ml/100 g i.p of normal saline and groups II and III received 50 mg and 100 mg/kg SMSE i.p., respectively. Animals of group IV received indomethacin (10 mg/kg i.p.) and group V received the dual blocker BW-755C (100 mg/kg i.p.) Paw edema was induced by a single injection of 0.1 ml of 0.5% arachidonic acid in 0.2 M carbonate buffer (pH 8.4) into the right hind paw (subplantar) of rats 30 minutes after drug treatment. Hind paw volume was measured 1 hour after arachidonic acid injection.[15]

Analgesic Activity

Writhing in mice

The mice were randomly divided into four groups (6 mice/group). Mice of the first group (control) received normal saline (0.1 ml/10 g) i.p., the second group received 100 mg/kg i.p. ibuprofen and the third and fourth groups received 50 mg and 100 mg/kg i.p. SMSE, respectively. Thirty minutes later, each mouse was administered 0.1 ml/ 10 g i.p. of 1% acetic acid. Writhing response was observed by the method of Turner.[16] The time of onset of writhing and the number of writhing in 15 minutes were noted.

Tail clip method

It was done in mice by applying a metal artery clip at the base of the tail with its jaw sheathed with thin rubber tubing.[17] Those mice that did not show any effort to dislodge the clip within 15 seconds were rejected. The tail clip was applied 30, 60 and 90 minutes after i.p. administration of 50 mg/kg SMSE and 100 mg/kg SMSE i.p. Normal saline (0.1 ml/g i.p.) was used as control and 100 mg/kg i.p. of ibuprofen was

used as a reference analgesic agent. It was considered as a response if there was no attempt by the mouse to dislodge the clip within 15 seconds.

Tail- flick method

The antinociceptive effect of the test substance was determined by the tail-flick method described by Sewell and Spencer.[18] One to 2 cm of the tail of mice was immersed in warm water kept constant at 55 ± 1°C (Swan scientific instruments). The reaction time was the time taken by the mice to deflect their tails. The first reading is discarded and the reaction time was taken as a mean of the next two readings. Balb-C mice were randomly divided into four groups (six in each). Mice of group I (control) received normal saline (0.1 ml/10 g) i.p. and those of group II ibuprofen (100 mg/kg i.p.) and groups III and IV received 50 and 100 mg/kg i.p. of SMSE, respectively. Thirty minutes later, the tail was immersed in the water bath and tail flick response was recorded. The same experiments were carried out after 60 minutes and 120 minutes again.

Antipyretic Studies

Brewer's yeast-induced pyrexia

All experiments were conducted at a room temperature of 28 ± 1°C. Pyrexia was induced in rats by injecting Brewer's yeast (2 mg/kg i.p) following the method of Bruguerolle and Roucoules.[19] After 18 hours, those rats whose rectal temperature rose to a minimum of 101.3° F were selected and divided into three groups (n = 6). Group I (control) received normal saline (0.1 ml/100g i.p.) and groups II and III received 50 and 100 mg/kg i.p. of SMSE, respectively. Rectal temperature was recorded using a telethermometer (Aplab) first after 30 minutes and then after 60 minutes for the next 4 hours.

Effect on normal peritoneal cell

Seventy-two mice were divided into three groups of 24 mice in each group. While group I received 0.1 ml/10g i.p. normal saline, groups II and III received 50 and 100 mg/kg i.p. of SMSE, respectively. Total peritoneal exudate cells were counted from each group (six mice at a time) at 6, 12, 24 and 48 hours of treatment and compared.[20] The number of phagocytes was also determined by staining with 1% neutral red solution using a hemocytometer.

Statistical analysis

Data are presented as arithmetic mean ± S.E.M. of least six experiments. Statistical analysis was performed by one-way analysis of variance (ANOVA) followed by Dunnett's test or by Student's paired '*t*' test. "*P*" value <0.05 was considered statistically significant.

RESULTS

Acute Toxicity Studies

It was found that SMSE was non-toxic up to 1.2 g/kg, i.p. body weight up to 24 hours. The two doses of SMSE used in the study were 50 and 100 mg/kg i.p.

Anti-inflammatory Studies

Carrageenan-induced edema

SMSE inhibited carrageenan-induced paw edema by 56.8% at a dose of 50 mg/kg and 68% at the dose of 100 mg/kg i.p. that were more than the 50% inhibition produced by ibuprofen, the standard drug [Table 1].

Croton oil-induced ear inflammation

SMSE inhibited croton oil-induced ear inflammation in mice. While it inhibited the inflammation by 7.35% at a dose of 50 mg/kg, the higher dose of 100 mg/kg SMSE produced an inhibition of 47.06% that was comparable to the 54.4% inhibition produced by the standard drug ibuprofen [Table 1].

Cotton pellet-induced granuloma

The increase in the dry weight of cotton pellet granuloma was compared with the control. It was found that 50 mg/kg i.p. of SMSE produced 28.29% inhibition of the increase in dry weight and 100 mg/kg i.p. SMSE produced 42.86% inhibition. However, ibuprofen, the standard drug, could produce only 14.29% inhibition in this model [Table 1].

Freund's adjuvant induced polyarthritis

SMSE inhibited polyarthritis in rat and this effect did not increase with the increase in dose. In fact, the effect produced by the lower dose of SMSE i.e. 50 mg/kg i.p. i.e. 53.79% inhibition was more than the 38.62% inhibition produced by the higher dose of 100 mg/kg i.p. and the effect produced by 50 mg/kg SMSE was a little more than the 50.69% inhibition produced by ibuprofen [Table 1].

Table 1: Effect of *Swietenia mahagoni* seed extract on four different models of inflammation

Drug	Dose (i.p.)	Carrageenan-induced paw edema (volume in ml)	Croton oil-induced ear inflammation (mg)	Increase in cotton pellet wt. (mg)	Freund's adjuvant-induced arthritis (volume in ml)
N. Saline	0.1 ml/100 g	0.44 ± 0.22	68 ± 2.137	70 ± 1.832	0.29 ± 0.034
Ibuprofen	100 mg/kg	0.22 ± 0.036*	31 ± 1.719*	60 ± 1.832*	0.143 ± 0.029*
SMSE	50 mg/kg	0.19 ± 0.048*	63 ± 1.511	50 ± 3.419*	0.134 ± 0.011*
SMSE	100 mg/kg	0.14 ± 0.016*	36 ± 1.719*	40 ± 1.814*	0.178 ± 0.02*

Data are expressed as mean ± SEM. Statistical analysis was done by one-way analysis of variance (ANOVA) followed by Dunnett's test or by Student's *t*-test. *Significant inhibition as compared to control (*P* <0.05).

Arachidonic acid-induced paw edema

Arachidonic acid injection (subplantar) in right hand paw produced significant edema after 1 hour. Indomethacin, the cyclo-oxygenase blocker, inhibited it by 16.09%, whereas BW755C, the dual blocker, inhibited it by 83.90 %. SMSE at doses of 50 and 100 mg/kg inhibited the edema by 53.64% and 71.45 %, respectively, which suggested that the extract behaved like BW755C [Table 2].

Analgesic Effects

Writhing in mice

SMSE (100 mg/kg i.p.) significantly reduced acetic acid-induced writhing in mice in a time-dependent manner [Table 3]. SMSE was more effective than ibuprofen in this activity [Table 3].

Tail clip test

Significant analgesic activity was shown by SMSE in a time-dependent manner and the effect of both the doses of SMSE tested was more than that produced by the standard drug, ibuprofen (data not shown).

Tail flick test

SMSE showed significant analgesic activity in this model also and the effect was time dependent. On a weight-to-weight basis, the analgesic activity of SMSE was more than that produced by ibuprofen, the standard agent (data not shown).

Antipyretic study

Brewer's yeast at a dose of 2 mg/kg i.p. increased the rectal temperature by ~1°F. SMSE up to 100 mg/kg i.p. did not show any significant antipyretic activity.

Effect on normal peritoneal cell

It was observed that the average number of macrophages was increased after SMSE treatment in a dose-depedent manner as compared to the control [Table 4].The linear increase was effective up to 24 hours and then on the 48th hour the count came down [Table 4].

Table 2: Effect of *Swietenia mahagoni* seed extract on arachidonic acid induced paw oedema in rats

Drug	Dose (i.p.)	Difference in paw volume in ml (% Inhibition as compared to saline control)
N. Saline	0.1 ml/100g	4.66 ± 0.423
Indomethacin	10 mg/kg	3.91 ± 0.714 (16.09)
BW755C	100 mg/kg	0.75 ± 0.112 *(83.90)
SMSE	50 mg/kg	2.16 ± 0.248 *(53.64)
SMSE	100 mg/kg	1.33 ± 0.211 *(71.45)

Statistical analysis was done by one-way analysis of variance (ANOVA) followed by Dunnett's test or by Student's *t*-test. *Significant inhibition as compared to control (P <0.05).

Table 3: Effect of *Swietenia mahagoni* seed extract on acetic acid induced writhing in mice

Drug	Dose (i.p.)	Number of writhing (mean ± SEM)
N. Saline	0.1 ml/10g	33.33 ± 2.11
Ibuprofen	100 mg/kg	9.2 ± 0.78*
SMSE	50 mg/kg	13.66 ± 2.11*
SMSE	100 mg/kg	8.1 ± 1.40*

Statistical analysis was done by one-way analysis of variance (ANOVA) followed by Dunnett's test or by Student's t-test. *Significant inhibition as compared to control (P <0.05).

DISCUSSION

The present study revealed that SMSE possesses significant anti-inflammatory and analgesic activity in experimental animals at doses of 50 and 100 mg/kg i.p. The anti-inflammatory effect of SMSE could be observed in acute (carrageenan and arachidonic acid-induced paw edema in rat and croton oil-induced ear inflammation in mice), sub-chronic (cotton pellet-induced granuloma in rat) and chronic (Freund's complete adjuvant-induced polyarthritis in rat) models of inflammation. Since SMSE inhibited edema similar to that of the dual-blocker BW755C in arachidonic acid induced-paw edema in rat and since indomethacin failed to show any significant inhibitory effect in this model, it is plausible that SMSE reduced inflammation by blocking both the lipo-oxygenase and cyclo-oxygenase pathways of arachidonic acid metabolism. The observation that SMSE significantly reduced inflammation in the Freund's adjuvant-induced polyarthritis in rat reveals that SMSE possesses anti-arthritic activity as well. It is interesting to note that in all models of inflammation, the effect produced by 100 mg/kg i.p. of SMSE was either more than or comparable to that produced by 100 mg/kg i.p. of ibuprofen, the standard NSAID.

While SMSE reduced acetic acid-induced writhing significantly it also showed analgesic activity in tail clip and tail flick models of analgesia in a time- and dose-dependent manner in comparison to ibuprofen, the reference anti-inflammatory agent. The extract did not possess significant antipyretic activity.

Table 4: Effect of *Swietenia mahagoni* seed extract on macrophage cell count in mice

Drug	Dose (i.p.)	Number of macrophages × 10^4			
		6 hours	12 hours	24 hours	48 hours
N. Saline	0.1 ml/10g	122 ± 10.51	120 ± 9.87	123 ± 10.23	119 ± 9.26
SMSE	50 mg/kg	151 ± 9.98	201 ± 23.42*	345 ± 12.32*	304 ± 15.33*
SMSE	100 mg/kg	180 ± 7.1	240 ± 11.5*	458 ± 13.24*	417 ± 7.0*

Statistical analysis was done by one-way analysis of variance (ANOVA) followed by Dunnett's test or by Student's *t*-test. *Significant inhibition as compared to control (P <0.05).

To evaluate whether SMSE treatment has any effect on cell growth, the effect of SMSE was evaluated on the peritoneal exudate cells of normal mice. Normally each mouse contains about 5×10^6 intraperitoneal cells (similar to the observation in the present study), 50% of which are macrophages. SMSE treatment enhanced the peritoneal cell count and also the number of macrophages. Nonspecific accumulation of macrophages occurs in the peritoneal cavity after injection of certain materials such as casein, Freund's complete adjuvant, and thioglycolate. Mature macrophages in the untreated peritoneal cavity are mostly residential. Intraperitoneal injection of different agents leads to exudation and intraperitoneal accumulation of new macrophages, which differ from mature macrophages. It has been reported that generally the exudate macrophages are more active than the residential mature ones in their ability to spread on the surface to which the cells are attached, receptor size of the cell coat, response to chemotactic stimuli, and composition of cell wall.[21] Though the actual role of SMSE in the enhancement of peritoneal cell count and macrophage count cannot be explained at the present juncture, it is possible that SMSE may also alter the immune response along with the anti-inflammatory effect. However, the cellular inflammatory ratio (neutrophil–macrophage–lymphocyte) needs to be assessed in the presence of SMSE to substantiate such a possibility. In this connection, it is worth mentioning that enhancement of peritoneal cell count and the number of macrophages in normal mice has been reported to occur with compounds possessing anti-inflammatory properties.[22,23]

It is well known that there is a close relationship between inflammation and cancer.[24,25] It has been reported that tumor promoters recruit inflammatory cells to the application site and cancer development may also act by aggravating inflammation in the tissue and vice versa and that inflammatory cells are capable of inducing genotoxic effects.[26] So it is likely SMSE may possess anti-tumor activity as well.

REFERENCES

1. Ali BH, Blunden G. Pharmacological and toxicological properties of Nigella sativa. Phytother Res 2003;17:299-305.
2. Kweifio-Okai G. Antiinflammatory activity of a Ghananian antiarthritic herbal preparation: I. J Ethnopharmacol 1991;33:263-7.
3. Kweifio-Okai G. Antiinflammatory activity of a Ghananian antiarthritic herbal preparation: II. J Ethnopharmacol 1991;33:129-33.
4. Razdan MK, Kapila K, Bhide NK. Antifertility effect and some pharmacological actions of Butea frondosa seed extracts. Indian J Physiol Pharmacol 1969;13:239-49.
5. Odukoya OA, Houghton PJ, Raman A. Lipoxygenase inhibitors in the seeds of Aframomum danielli K. Schum (Zingiberaceae). Phytomed 1999;6:251-56.
6. Hosseinzadeh H, Haddadkhodaparast MH, Arash AR. Antinociceptive, antiinflammatory and acute toxicity effects of Salvia leriifolia Benth seed extract in mice and rats. Phytother Res 2003;17:422-25.
7. Wei F, Ma LY, Jin WT, Ma SC, Han GZ, Khan IA, *et al.* Antiinflammatory triterpenoid saponins from the seeds of Aesculus chinensis. Chem Pharm Bull (Tokyo) 2004;52:1246-48.
8. Ekimoto H, Irie Y, Araki Y, Han GQ, Kadota S, Kikuchi T. Platelet aggregation inhibitors from the seeds of Swietenia mahagoni: inhibition of *in vitro* and *in vivo* platelet- activating factor-induced effects of tetranortriterpenoids related to swietenine and swietenolide. Planta Med 1991;57:56-8.
9. Rahman AK, Chowdhury AK, Ali HA, Raihan SZ, Ali MS, Nahar l, *et al.* Antibacterial activity of two limonoids from Swietenia mahagoni against multiple-drug-resistant (MDR) bacterial strains. Nat Med (Tokyo) 2009;63:41-5.
10. Ghosh MN. Fundamentals of experimental pharmacology, second ed. Calcutta, India: Scientific Book Agency; 1984.
11. Winter CA, Risely EA, Nuss GW. Carrageenin induced edema in hind paw of the rat as an assay for antiinflammatory drugs. Pro Soc Exp Biol Med (NY) 1962;111:544-7.
12. D'Arcy PF, Howard EM, Muggleton PW, Townsend SB. The anti-inflammatory action of griseofulvin in experimental animals. J Pharm Pharmacol 1960;12:659-65.
13. Brooks RR, Bonk KR, Decker GE, Miller KE. Anti-inflammatory activity of orpanoxin administered orally and topically to rodents. Agents and Actions 1985;16:369-76.
14. Newbould BB. Chemotherapy of arthritis induced in rats by mycobacterial adjuvant. Br J Pharmacol Chemother 1963;21:127-36.
15. DiMartino MJ, Campbell GK Jr, Wolff CE, Hanna N. The Pharmacology of arachidonic acid- induced rat paw oedema. Agents Actions 1987;21:303-5.
16. Turner RA. Screening methods in pharmacology. New York: Academic Press, Inc; 1965. p. 1.
17. Palanichamy S, Nagarajan S. Analgesic activity of Cassia alata leaf extract and kaempferol 3-o-sophoroside. J Ethnopharmacol 1990;29:73-8.
18. Sewell RD, Spencer PS. Antinociceptive activitiy of narcotic agonist and partial agonist analgesics and other agents in the tail-immersion test in mice and rats. Neuropharmacol 1976;15:683-8.
19. Bruguerolle B, Roucoules X. Time-dependent changes in body temperature rhythm induced in rats by brewer's yeast injection. Chronobiol Int 1994;11:180-6.
20. Hudson L, Hay FC. Practical Immunology. 3rd ed. Oxford: Blackwell Scientific Publications; 1989.
21. Den otter W, De Groot JW, Van Basten CD, Rademakers LH, De Wager RA, Pels E. Brewer thioglycollate medium induces different exudates in guinea pigs and mice. Exp Mol Pathol 1982;36:403-13.
22. Besra SE, Sharma RM, Gomes A. Antiinflammatory effect of petroleum ether extract of leaves of Litchi chinensis Gaertn. (Sapindaceae). J Ethnopharmacol 1996;54:1-6.
23. Sur P, Das M, Gomes A, Vedasiromoni JR, Sahu NP, Banerjee S *et al.* Trigonella foenum graecum (fenugreek) seed extract as an antineoplastic agent. Phytother Res 2001;15:257-9.
24. Thun M, Namboodiri MM, Heath CW Jr. Aspirin use and reduced risk of fatal colon cancer. N Engl J Med 1991;325:1593-6.
25. DuBois RN, Giardiello FM, Smalley WE. Nonsteroidal anti-inflammatory drugs, eicosanoids and colorectal cancer prevention. Gastroenterol Clin North Am 1996;25:773-91.
26. Rosin MP, Anwar WA, Ward AJ. Inflammation, chromosomal instability, and cancer: The schistosomiasis model. Cancer Res 1994;54:1929-33.

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