International Journal of Pharmacology

ISSN 1811-7775

science alert

ansinet
Asian Network for Scientific Information

International Journal of Pharmacology 4 (2): 88-94, 2008
ISSN 1811-7775

Studies on Antipyretic-Analgesic and Ulcerogenic Activity of Polyherbal Preparation in Rats and Mice

[1]M. Gupta, [1]B.P. Shaw and [2]A. Mukerjee
[1]Institute of Post Graduate Ayurvedic Education and Research,
294/3/1, APC Road, Kolkata-700009, India
[2]Division of Pharmaceutical Technology, Department of Chemical Technology,
Calcutta University, 92, APC Road, Kolkata-700009, India

Abstract: The aqueous extract of polyherbal Ayurvedic preparation PD-10 (from the roots of *Hemidesmus indicus* R. Br. (Asclepiadaceae), *Rubia cordifolia* L. (Rubiaceae), *Cissampelos pareira* L. (Menispermaceae); fruits of *Terminalia chebula* Retz. (Combretaceae), *Emblica officinalis* Gaertn. (Euphorbiaceae), *Terminalia bellirica* Roxb. (Combretaceae), *Vitis vinifera* L. (Vitaceae), *Grewia asiatica* L. (Tiliaceae), *Salvadora persica* L. (Salvadoraceae) and granules of *Saccharum officinarum* L. (Poaceae)) was investigated for antipyretic property. The extract caused significant ($p<0.05$) antipyretic activity induced pyrexia by using Brewer's yeast in rats. The evaluation of analgesic activity of PD-10 using acetic acid induced writhing model, hot plate method and tail immersion methods in mice revealed very significant ($p<0.01$) analgesic activity. The ulcerogenicity effect of PD-10 studied at different dosages by Barret's method in rats showed significantly lesser ulcer effect even at very high dosage as compared to that of aspirin. These data confirm the antipyretic, analgesic and ulcerogenic properties of the polyherbal Ayurvedic preparation (PD-10) as enunciated in the traditional texts.

Key words: Polyherbal preparation, antipyretic, analgesic, anti-ulcerogenic

INTRODUCTION

Antipyretic-analgesics and more particularly the non-steroidals account for the largest class of medication in demand worldwide. However, use of most of these formulations has been associated with gastrointestinal, renal, hepatic, central nervous system and dermatological effects (Simon, 1995; Suleyman *et al*., 2007). On the other hand, traditional Indian systems of medicine, such as Ayurveda are based on holistic treatment of diseases, primarily relying on natural herbal drugs. Ayurvedic literatures like Charak Samhita provide a rich text for herbal drugs that are available till today. This indicated the possibility to explore into the literatures and concepts of holistic Ayurvedic medication systems for some antipyretic-analgesic preparations with lesser untoward effects.

According to Ayurveda, pyrexia originates from a combination of indigestion, seasonal variations and significant alterations in daily routine. Charak has defined the ten antipyretic drugs in Jwarhar Mahakashay Sutra Sthana of Charak Samhita (Shastri, 1988). Most Ayurvedic preparations are polyherbal in nature to take care of the multiple components of disease conditions. This *Jwarhar Mahakashay* group of antipyretic drugs includes Sariva (*Hemidesmus indicus* R. Br.), Manjistha (*Rubia cordifolia* L.), Patha (*Cissampelos pareira* L.), Haritaki (*Terminalia chebula* Retz.), Amala (*Emblica officinalis* Gaertn.), Vibhitak (*Terminalia bellirica* Roxb.), Draksha (*Vitis vinifera* L.), Parushak (*Grewia asiatica* L.), Peelu (*Salvadora persica* L.) and Sharkara (*Saccharum officinarum* L.) plants. These medicinal plants have been in traditional usage for treatment of pyrexia as detailed in ancient Ayurvedic texts like Charak Samhita and Susruta Samhita. Many of these medicinal plants have been individually reported to exhibit diverse pharmacological actions such as anti-inflammatory, analgesic, hepato-protective, anti-microbial and antiulcer properties as shown in Table 1 (Nijveldt *et al*., 2001; Anoop and Jagadeesan, 2003; Perianayagam *et al*., 2004; Ledon *et al*., 2003; Kasture *et al*., 2001; Saito *et al*., 1998; Monforte *et al*., 2001; Anand *et al*., 1994; Valsaraj *et al*., 1997; Asmawi *et al*., 1993; Gulati *et al*., 1995). Analysis of the

Corresponding Author: Dr. Mradu Gupta, Department of Dravyaguna,
Institute of Post Graduate Ayurvedic Education and Research, 294/3/1,
APC Road, Kolkata-700009, India Tel: 91-33-24614461, 91-9433665125

Table 1: Pharmacological properties and chemical constituents of Jwarhar Mahakashay drugs

Name	Scientific name	Family	Parts used	Pharmacological properties reported	Active chemical constituents
Sariva	*Hemidesmus indicus* R. Br.	Asclepiadaceae	Roots	Anti-inflammatory, Anti-ulcer	Flavonoids, triterpenoids, tannin, phytosterol, β-sitosterol
Sharkara	*Saccharum officinarum* L.	Poaceae	Granules	Anti-inflammatory, analgesic	Flavonoids, glucosides, glycans, glucose, sucrose, phenols
Patha	*Cissampelos pareira* L.	Menispermaceae	Roots	Tumour-inhibitor	Alkaloids, berberin, hayatine, cissampareine
Manjistha	*Rubia cordifolia* L.	Rubiaceae	Fruits	Anti-inflammatory, anti-bacterial	Glycosides, anthraquinone, rubiadin, triterpenes
Draksha	*Vitis vinifera* L.	Vitaceae	Fruits	Anti-ulcer, hepatoprotective	Flavonoids, glucose, fructose, glycosides, polyphenols
Peelu	*Salvadora persica* L.	Salvadoraceae	Fruits	Anti-ulcer, anti-microbial	Tannin, salvadorin, glucose, fructose
Parushak	*Grewia asiatica* L.	Tiliaceae	Fruits	Anti-malarial, anti-ulcer	Flavonoids, tannin, glucose, glycosides
Haritaki	*Terminalia chebula* Retz.	Combretaceae	Fruits	Anti-microbial, purgative	Tannin, triterpenes, chebulinic acid, glycosides
Vibhitak	*Terminalia bellirica* Roxb.	Combretaceae	Fruits	Hepato-protective, anti-histaminic	Gallic acid, glycosides, chebulagic acid, triterpenoids
Amala	*Emblica officinalis* Gaertn.	Euphorbiaceae	Fruits	Anti-ulcer, anti-inflammatory, hepato-protective	Vitamin C, elagic acid, polyphenol, glucose, phyllembin

chemical constituents of these plants revealed the presence of tannins, triterpenoids, phenols, glycosides, sucrose, glucose, flavonoids and flavonidic glycosides as shown in Table 1 (Sharma *et al*., 2001; Kirtikar and Basu, 1984; Baltenweck-Guyot *et al*., 2000; Foo *et al*., 1998; Kundu and Mahato, 1993). However, there was no scientific evaluation of the antipyretic-analgesic effect of this traditional polyherbal Ayurvedic preparation till now even though it was observed to be inhibiting the pyretic ignition mechanism and was clinically effective. The current research intends to systematically evaluate the antipyretic and analgesic activity as well as the acute gastrointestinal toxicity of such a polyherbal preparation made following Ayurvedic literature in rodent experiments.

MATERIALS AND METHODS

Preparation of polyherbal extract (PD-10): The roots of Sariva (*Hemidesmus indicus* R. Br.), Manjistha (*Rubia cordifolia* L.) and Patha (*Cissampelos pareira* L.), fruits of Haritaki (*Terminalia chebula* Retz.), Amala (*Emblica officinalis* Gaertn.), Vibhitak (*Terminalia bellirica* Roxb.), Draksha (*Vitis vinifera* L.), Parushak (*Grewia asiatica* L.) and Peelu (*Salvadora persica* L.) and Sharkara granules (*Saccharum officinarum* L.) were obtained from the Apothecary department of the Institute of Post Graduate Ayurvedic Education and Research, Kolkata during May 2006. These were authenticated and identified by the Department of Ethnobotany, Botanical Survey of India, Shibpur, Howrah and a voucher specimen was deposited in the herbarium before their utilization (Table 1). Plant parts were shade dried and coarsely powdered up to 40 mesh size. Equal portions by weight of all ingredients were homogenously mixed and subjected to soxhlet extraction in refluxing distilled water. The extraction was continued for 48 h using distilled water four times by weight of the crude drug mixture. The aqueous extract was filtered through calico cloth and was further concentrated to solid under reduced pressure over water bath in a rotary evaporator. The extract yield from 300 g of plant powder mixture was 75 g. This Jwarhar Mahakashay preparation was termed PD-10 for all systematic evaluation studies and preserved at the Division of Pharmaceutical Technology Laboratory, Department of Chemical Technology, Calcutta University, Kolkata, where the experimental studies were carried out during 2006-07.

Experimental animals: Colony bred Swiss albino mice (20-25 g) and Wister rats (120-130 g) obtained from the Indian Institute of Chemical Biology (I.I.C.B.), Kolkata were used for this study. They were housed in polypropylene cages in the well-ventilated animal house facility of the Department of Chemical Technology, Calcutta University, Kolkata. The animals were maintained with standard pellet diet and potable water *ad libitum*. They were then divided in seven groups of six each for the five different test drug (PD-10) dosage groups, the standard (Aspirin/Morphine sulphate) group and the control (saline) group. For all pharmacological evaluations including toxicity studies, prior approval was obtained from the Animal Ethics Committee under the faculty of Chemical Technology of Calcutta University (Reg. No. 506/01/a/CPCSEA Dt. 31.10.2001).

Test drugs: Aspirin and Morphine Sulphate procured from M/s Dey's Medical Stores, Kolkata were used as standard drugs and PD-10 was used in different oral dosage for comparison of efficacy. Normal saline has served as the vehicle control.

Phytochemical analysis: Standard phytochemical test was used in screening the extract for different constituents. Briefly, $FeCl_3$ test was used to characterize for tannins and salicylates, Dragendorff's reaction and Mayer's test was used for alkaloids and Fehling's test was used for reducing sugars. Similarly, HCl-Magnesium test was used for flavonoids while frothing test was deployed for saponins and the Liebermann - Buchard reaction was used for detecting the presence of triterpenoids and steroids (Sawadogo *et al*., 2006b; Furniss *et al*., 1989).

Toxicity studies: Acute toxicity was estimated following the graphical method of Litchfield and Wilcoxon (1949) in mice. Different doses for test drug PD-10 extract (1000, 2000, 4000, 6000 and 8000 mg kg^{-1}) were administered p.o. to 5 groups of 6 Swiss albino mice each. The Control group received normal saline (5 mL kg^{-1} p.o.). Animals were under observation for 72 h, during which their behavioral patterns were noted and signs of toxicity recorded. All deaths occurring during the first 24 h were meticulously noted.

Antipyretic activity studies on PD-10: The antipyretic activity was evaluated in Brewer's yeast induced pyretic model in rats (Hajare *et al*., 2000; Ghosh, 1984). All the Wister rats were fasted for 12 h water ad libitum and then divided into seven homogenous groups. Saline (0.5 mL) was administered orally to the control group, Aspirin (100 mg kg^{-1}) p.o. was given to the standard group while the five drug treated groups were administered with 100, 200, 300, 400 and 500 mg kg^{-1} body wt of the test drug PD-10 p. o. respectively. The rectal temperatures of all the animals were noted down at the beginning of the experiment. Each animal was given the prescribed drug p.o. and was immediately injected with 10 mL kg^{-1} of 15% w/v yeast solution in water subcutaneously to induce fever. The rectal temperature was thereafter noted in degrees Centigrade at the end of 1, 2, 3, 4 and 24 h.

Analgesic activity studies on PD-10: The central analgesic activity against thermal stimulus was recorded in mice following hot plate method as well as tail immersion method (Hajare *et al*., 2000; Ghosh, 1984). Morphine sulphate (2.5 mg kg^{-1}, i.m.) was used as a standard drug. The test drug PD-10 dissolved in water was administered p.o. in doses of 100, 200, 300, 400 and 500 mg kg^{-1} body wt to different drug groups 1 h before applying the thermal stimulus, which was maintained at 55±0.2°C. The latency in hind paw licking and clear tail withdrawal were recorded as responses after 10, 30 and 60 min of drug administration in the hot plate method and tail immersion methods respectively. Maximum reaction time of observation was about 60 sec throughout to avoid tissue damage.

The peripheral analgesic activity of PD-10 was evaluated in acetic acid induced writhing experiments in mice. The abdominal constriction writhings resulting from intraperitoneal injection of acetic acid (10 mL kg^{-1} of 0.6% v/v glacial acetic acid solution in water) were recorded according to standard procedure (Veerappan *et al*., 2005; Nwafor and Okwuasaba, 2003). The animals were divided into seven groups of 6 mice each. The test drug PD-10 dissolved in water was administered i.p. in doses of 100, 200, 300, 400 and 500 mg kg^{-1} body wt to the five test drug groups, while saline was administered to the control group. Aspirin (100 mg kg^{-1} p.o.) was used as the standard drug for comparison. Acetic acid solution was administered after 30 min and number of writhings counted in each animal for 15 min. Percentage inhibition response was calculated as the reduction in the number of abdominal constrictions between control group and test drug treated groups as a percentage of the number of wriths observed in case of the control group.

Assessment for ulcerogenic effect: Acute ulcerogenicity was evaluated in Wister rats divided in 6 groups, housed in individual cages and fasted for 24 h prior to administration of the test drug or aspirin (Shay *et al*., 1945). Four drug-treated groups were administered with the experimental drug PD-10 in p.o. doses of 200, 500, 1000 and 1500 mg kg^{-1}, respectively. Aspirin was administered at 200 mg kg^{-1} p.o. dose. Animals were euthanited after 12 h of drug treatment, abdomen was opened and the stomach was cut open along the greater curvature (Rifat-uz-Zaman *et al*., 2006). The stomach content was cleaned and washed with saline. The mucosal surface was examined by two independent observers. The degree of ulceration was graded from zero to five (0-5) depending on the size and severity of ulcers (Barret *et al*., 1953).

Statistical analysis: All values were expressed as mean±SEM. Analysis of variance was performed by ANOVA procedures (Pipkin and Livingstone, 1984). Differences were considered statistically significant at $p<0.05$ and very significant at $p<0.01$.

RESULTS

Phytochemical analysis: Phytochemical analysis of the PD-10 extract revealed the presence of tannins, reducing sugars, flavonoids, glycosides and salicylates.

Toxicity study: Detailed studies revealed very low toxicity and nil mortality even at very high dosage of 8000 mg kg^{-1} b.wt. during acute toxicity tests. During initial period (up to 4 h), the higher test dose (6000 and

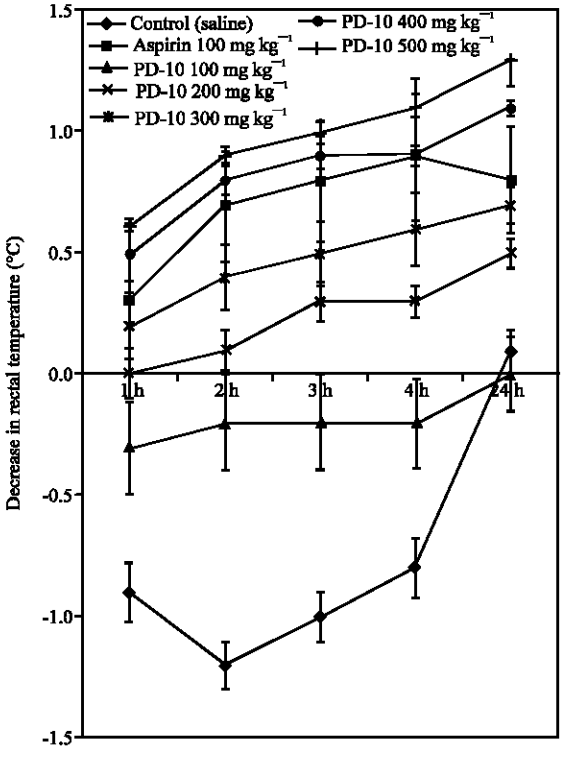

Fig. 1: Decrease in average rectal temperature w.r.t. initial temperature. Vertical bars are mean±SEM (n = 6)

8000 mg kg^{-1}) treated animals showed some symptoms of decreased motor activity and respiratory distress. The animals recovered thereafter and no mortality was recorded.

Antipyretic activity of PD-10 in rats: The Antipyretic effect for p.o. administration of PD-10 was dose dependent and the response at 400 and 500 mg kg^{-1} dosages was more pronounced compared to that of 100 mg kg^{-1} p.o. aspirin (Fig. 1). Marked antipyretic response for PD-10 at 400 and 500 mg kg^{-1} p.o. dosages was observed ($p<0.05$) even at 24 h of treatment. The polyherbal preparation PD-10 has proved to be significantly antipyretic in Brewer's Yeast pyrexia model.

Analgesic activity in mice: Table 2 and 3 shows the analgesic activity due to thermal stimulus following hot plate analgesia and tail immersion methods in mice. The central analgesic activity was found to be comparatively weaker at lower dosages of the test drug as compared to the standard drug (morphine sulphate). However, the nociceptive response at 400 and 500 mg kg^{-1} dosage of PD-10 ($p<0.01$) was quite comparable to that of morphine sulphate.

Table 2: Average reaction time in hot plate method

Group	Dose (mg kg^{-1}) p.o.	10 min	30 min	60 min
Control (saline)		5.750±0.438	5.433±0.235	6.333±0.329
Morphine	2.5	9.483±0.291[a]	11.150±0.411[a]	11.017±0.297[a]
PD-10	100.0	5.883±0.386	5.983±0.224	6.833±0.312
PD-10	200.0	6.350±0.231[b]	6.517±0.221[b]	7.533±0.267[b]
PD-10	300.0	7.233±0.300[b]	7.433±0.288[a]	9.733±0.297[a]
PD-10	400.0	9.333±0.274[a]	9.700±0.376[a]	10.533±0.229[a]
PD-10	500.0	10.250±0.217[a]	11.767±0.426[a]	12.383±0.368[a]

Significance relative to control: a: $p<0.001$, b: $p<0.01$, c: $p<0.1$ (ANOVA test); Values represent mean±SEM (n = 6)

Table 3: Average reaction time in tail immersion method

Group	Dose (mg kg^{-1}) p.o.	10 min	30 min	60 min
Control (saline)		5.083±0.384	5.183±0.368	5.133±0.384
Morphine	2.5	9.917±0.280[a]	10.117±0.256[a]	10.817±0.412[a]
PD-10	100.0	5.783±0.438	5.817±0.428	5.983±0.490
PD-10	200.0	6.017±0.187	6.300±0.188[b]	6.600±0.153[b]
PD-10	300.0	6.433±0.263	6.950±0.543[b]	7.067±0.599[b]
PD-10	400.0	8.517±0.289[a]	9.100±0.310[a]	9.500±0.350[a]
PD-10	500.0	10.650±0.284[a]	11.233±0.336[a]	11.367±0.331[a]

Significance relative to control: a: $p<0.001$, b: $p<0.01$, c: $p<0.1$ (ANOVA test); Values represent mean±SEM (n = 6)

Table 4: Effects of PD-10 and aspirin on writhing induced by acetic acid in mice

Group	Dose (mg kg^{-1}) i.p.	No. of writhings	Inhibition (%)
Control (saline)	-	5.33±0.42	-
Aspirin	100	3.67±0.21[b]	31.3
PD-10	100	4.17±0.17[c]	21.9
PD-10	200	3.83±0.31[c]	28.1
PD-10	300	3.67±0.21[b]	31.3
PD-10	400	3.33±0.21[b]	37.5
PD-10	500	2.67±0.21[a]	50.0

Significance relative to control: a: $p<0.001$, b: $p<0.01$, c: $p<0.1$ (ANOVA test); Values represent mean±SEM (n = 6)

Table 5: Effects of PD-10 and aspirin on ulceration in rats

Group	Dose (mg kg^{-1}) p.o.	Score for degree of ulceration
Control (saline)	-	1.33±0.21
Aspirin	200	3.00±0.26[a]
PD-10	200	1.67±0.21[b]
PD-10	500	1.83±0.31[a]
PD-10	1000	2.17±0.31
PD-10	1500	2.50±0.22[a]

Significance relative to control: a: $p<0.001$, b: $p<0.01$, c: $p<0.1$ (ANOVA test); Values represent mean±SEM (n = 6)

Peripheral analgesia response due to oral doses of PD-10 was very significant ($p<0.01$) at 300, 400 and 500 mg kg^{-1} p.o. dosage and was more pronounced than aspirin p.o. dosage of 100 mg kg^{-1} (Table 4). Significant dose dependant inhibition of control writhes were observed at 100, 200, 300, 400 and 500 mg kg^{-1} p.o. doses of PD-10 and compared well in range with aspirin p.o. dosage of 100 mg kg^{-1}.

Acute ulcerogenicity in rats: Results of acute ulcerogenicity were studied in rats and the results were shown in Table 5. PD-10 exhibited almost negligible

ulcerogenicity at dosage of 200 and 500 mg kg^{-1}. Ulcerogenic responses due to 1000 and 1500 mg kg^{-1} p.o. dosage of PD-10 were also markedly low as compared to aspirin dosage of 200 mg kg^{-1}.

DISCUSSION

The polyherbal Ayurvedic preparation PD-10 exhibited marked antipyretic effect in yeast pyrexia model and the response is dose-dependent. Oral doses of PD-10 at 300, 400 and 500 mg kg^{-1} produced significant antipyretic effect in test animals. Fever is known to be associated with the production of prostaglandins in the hypothalamus (Okokon *et al*., 2008). Yeast pyrexia is generally associated with prostaglandin's responses in later hours (4 h) of yeast treatment, while the initial (1 to 4 h) pyrexia response is associated with a number of factors including the presence of histamine and bradikinin. Marked and sustained antipyretic response due to PD-10 is perhaps indicative of a prostaglandin receptor mediated response (Bennett and Plum, 1996).

The central analgesic effect of PD-10 was found to be weaker at lower dosage (100, 200 and 300 mg kg^{-1}) as compared to the standard drug, morphine sulphate. However, the central analgesic activity of PD-10 was quite pronounced and noticeable at higher doses (400 and 500 mg kg^{-1}) and comparable to the standard drug. The results of both hot plate method and tail immersion method indicate very significant ($p<0.01$) central analgesic activity in PD-10. The thermal test is sensitive to strong analgesics (Ibironke and Ajiboye, 2007) and the test drug response was dose-dependent, especially at higher ranges.

PD-10 inhibited acetic acid induced writhing in mice ($p<0.01$). Percentage reduction in normal acetic acid writhings was highly pronounced at 300, 400 and 500 mg kg^{-1} p.o. doses of test drug (31.3, 37.5 and 50.0%) when compared with pure compound aspirin (31.3 %). The abdominal contractions (writhings) were directly related to peripheral responses due to prostaglandins. Therefore, PD-10 components exhibited pronounced inhibitory responses either in synthesis, release or receptor reactions in prostaglandin mediated effects. Nociceptive response due to the test drug, although dose dependent, was pronounced at higher dosages and comparable to that of morphine (2.5 mg kg^{-1} i.m.). The ability of the extract to inhibit acetic acid-induced writhing in mice (a model of visceral pain) indicated that it could be useful in the management of visceral pain (Ibironke and Ajiboye, 2007). Components of PD-10, therefore, definitely possess some central analgesic responses.

Increased body temperature and pain are two major signs of the body against inflammation (Meli *et al*., 2001). A drug with anti-inflammatory activity usually also exhibits anti-pyretic and analgesic properties. The best examples would be the Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) which possess anti-inflammatory, analgesic and antipyretic properties (Perianayagam *et al*., 2004; Buffum and Buffum, 2000). Pronounced antipyretic action due to PD-10 possibly mediated through inhibition of prostaglandin production especially since the extract has been shown to exhibit analgesic and anti-inflammatory activities.

Preliminary phytochemical screening of the extract indicated the presence of tannins, reducing sugars, flavonoids, glycosides and salicylates. Of these, flavonoids are well known for their ability to inhibit pain perception (Sawadogo *et al*., 2006a) and to exhibit anti-inflammatory properties due to their inhibitory effects on enzymes involved in the production of the chemical mediator of inflammation (Oweyele *et al*., 2005). Flavonoids and its related compounds also exhibit inhibition of arachidonic acid peroxidation, which results in reduction of prostaglandin levels thus reducing the fever (Baumann *et al*., 1980). Since flavonoids exhibit several biological effects such as anti-inflammatory, anti-microbial, anti-hepato-toxic and anti-ulcer activities (Narayana *et al*., 2001; Nijveldt *et al*., 2001), it is likely that the antipyretic action of PD-10 preparation is primarily related to the presence of flavonoids.

PD-10 has proved to be very low ulcerogenic even in high p.o. doses of 1000 and 1500 mg kg^{-1} as compared to p. o. aspirin dosage of 200 mg kg^{-1}, validating its efficacy as a polyherbal therapeutic compound having minimal adverse side-effects as compared to standard non-steroidal antipyretic analgesic drugs. The low ulcerogenicity of the test drug could be primarily on account of the anti-ulcerogenic activity exhibited by many of its constituent plants as shown in Table 1 (Anoop and Jagadeesan, 2003; Saito *et al*., 1998; Monforte *et al*., 2001).

Antipyretic-analgesic action for PD-10 could be attributed to the presence of flavonoids in the constituent herbs, since flavonoids normally exhibit antipyretic, analgesic and anti-inflammatory properties. The preparation also proved to be much less ulcerogenic as compared to the standard Non steroidal anti inflammatory (NSAIDS) drugs. The extract PD-10 therefore continues to be used with significant success as an antipyretic compound in traditional clinical practice in several parts of India and the specific attributes ascribed to it in ancient Ayurvedic literature is thus justified and revaluated.

REFERENCES

Anand, K.K., B. Singh, A.K. Saxena, B.K. Chandan and V.N. Gupta, 1994. Hepatoprotective studies of a fraction from the fruits of *Terminalia bellerica* Roxb. on experimental liver injury in rodents. Phytother. Res., 8 (5): 287-292.

Anoop, A. and M. Jegadeesan, 2003. Biochemical studies on the anti-ulcerogenic potential of *Hemidesmus indicus* R. Br. Var. Indicus. J. Ethnopharmacol., 84 (2-3): 149-156.

Asmawi, M.Z., H. Kankaanranta, E. Moilaness and H. Vapaatalo, 1993. Anti-inflammatory activities of *Emblica officinalis* Gaertn. leaf extracts. J. Pharmacol., 45 (6): 581-584.

Baltenweck-Guyot, R., J.M. Trendel, P. Albrecht and A. Chaeffer, 2000. Glycosides and phenylpropanoid glycerol in *Vitis vinifera* cv. Gewürztraminer wine. J. Agric. Food. Chem., 48 (12): 6178-6182.

Barret, W.E., N. Rutledge, A.J. Plummer and F.F. Yonkman, 1953. Inhibition of ulcer formation in the Shay rat and reduction of gastric acidity in dogs by Antrenyl (oxyphenonium) (ba-5473) diethyl (2-hydroxyethyl) methylammonium bromide -phenyl-cyclohexaneglycolate, an anticholinergic agent. J. Pharmacol. Exp. Ther., 108 (3): 305-316.

Baumann, J., F. Von Brucchau Sen and G. Wurm, 1980. Flavonoids and related compounds as inhibition of arachidonic acid peroxidation. Prostaglandins, 20 (4): 627-639.

Bennett, J.C. and F. Plum, 1996. CECIL Textbook of Medicine, Prism Indian Edition. 20th Edn. 2: 1532-1535.

Buffum, M. and J.C. Buffum, 2000. Nonsteroidal anti-inflammatory drugs in the elderly. Pain Manage. Nurs., 1 (2): 40-50.

Foo, L.Y., Y. Lu and H. Wong, 1998. Biphenyl-linked biflavanoids from grape promace. Phytochemistry, 47 (6): 1137-1140.

Furniss, B.S., A.J. Hannaford, P.W.G. Smith and A.R. Tatchell, 1989. Vogel's Textbook of Practical Organic Chemistry, 5th Edn. Addison Wesley Longman Inc., pp: 1205.

Ghosh, M.N., 1984. Fundamentals of Experimental Pharmacology. Scientific Book Agency, Kolkata, pp: 153-157.

Gulati, R.K., S. Agarwal and S.S. Agarwal, 1995. Hepatoprotectic studies on *Phyllanthus emblica* Linn. and quercetin. Indian J. Exp. Biol., 33 (4): 261-268.

Hajare, S.W., S. Chandra, S.K. Tandon, J. Sharma, J. Lal and A.G. Telang, 2000. Analgesic and antipyretic activities of *Dalbergia sissoo* leaves. Indian J. Pharmacol., 32 (6): 357-360.

Ibironke, G.F. and K.I. Ajiboye, 2007. Studies on the anti-inflammatory and analgesic properties of *Chenopodium ambrosioides* leaf extract in rats. Int. J. Pharmacol., 3 (1): 111-115.

Kasture, S.B., V.S. Kasture and C.T. Chopde, 2001. Anti-inflammatory activity of *Rubia cordifolia* roots. J. Nat. Remedies, 1 (2): 111-115.

Kirtikar, K.R. and B.D. Basu, 1984. Indian Medicinal Plant. Lalit Mohan Basu M.B. (Ed.). Allahabad, India, 1: 95, 388, 607; 2: 1020, 1303, 1537; 3: 1596, 2221; 4: 2661.

Kundu, A.K. and S.B. Mahato, 1993. Triterpenoids and their glycosides from *Terminalia chebula*. Phytochemistry, 32 (4): 999-1002.

Ledon, N., A. Casaco, V. Rodriguez, J. Cruz, R. Gonzalez, Z. Tolon, M. Cano and E. Rojas, 2003. Anti-inflammatory and analgesic effect of a mixture of fatty acids isolated and purified from sugarcane wax oil. Planta Med., 69 (4): 367-369.

Litchfield, J.T. and F. Wilcoxon, 1949. A simplified method of evaluating dose-effect experiments. J. Pharmacol. Exp. Ther., 96 (2): 99-133.

Meli, R., E. Antonelli and G. Cirino, 2001. Analgesia and cyclo-oxygenase inhibitors. Digestive Liver Dis., 33 (Suppl. 2): S8-S11.

Monforte, M.T., N. Miceli, M.R. Mondello, R. Sanogo, A. Rossitto and E.M. Galati, 2001. Antiulcer activity of *Salvadora persica* on experimental ASA-induced ulcer in rats: Ultrastructural modifications. Pharma. Biol., 39 (4): 289-292.

Narayana, K.R., M.S. Reddy, M.R. Chaluvadi and D.R. Krishna, 2001. Bioflavonoids classification, pharmacological, biochemical effects and therapeutic potential. Indian J. Pharmacol., 33 (1): 2-16.

Nijveldt, R.J., E. Van Nood, D.E. von Hoorn, P.G. Boelens, K. Van Norren and P.A.M. Van Leeuwen, 2001. Flavonoids: A review of probable mechanisms of action and potential applications. Am. J. Clin. Nutr., 74 (4): 418-425.

Nwafor, P.A. and F.K. Okwuasaba, 2003. Anti-nociceptive and anti-inflammatory effects of methanolic extract of *Asparagus pubescens* root in rodents. J. Ethnopharmacol., 84 (2-3): 125-129.

Okokon, J.E., B.S. Antia and E. Umoh, 2008. Analgesic and anti-inflammatory effects of ethanolic root extract of *Hippocratea africana*. Int. J. Pharmacol., 4 (1): 51-55.

Oweyele, V.B., Y.Y. Oloriegbe, E.A. Balogun and A.O. Soladoye, 2005. Analgesic and anti-inflammatory properties of *Nelsonia canescens* leaf extract. J. Ethnopharmacol., 99 (1): 153-156.

Perianayagam, J.P., S.K. Sharma, A. Joseph and A.J.M. Christina, 2004. Evaluation of anti-pyretic and analgesic activity of *Emblica officinalis* Gaertn. J. Ethnopharmacol., 95 (1): 83-85.

Pipkin, F.B. and C. Livingstone, 1984. Medical Statistics Made Easy. Churchill Livingstone Inc., Edinburgh, pp: 70-75.

Rifat-uz-Zaman, M.S. Akhtar and M.S. Khan, 2006. Anti-ulcerogenic screening of *Cichorium intybus* L. leaf in Indomethacin treated rats. Int. J. Pharmacol., 2 (2): 166-170.

Saito, M., H. Hosoyama, T. Ariga, S. Kataoka and N. Yamaji, 1998. Antiulcer activity of grape seed extract and procyanindins. J. Agric. Food Chem., 46 (4): 1460-1464.

Sawadogo, W.R., A. Meda, C.E. Lamien, M. Kiendrebeogo, I. P. Guissou and O.G. Nacoulma, 2006a. Phenolic content and antioxidant activity of six acanthaceae from Burkina Faso. J. Biol. Sci., 6 (2): 249-252.

Sawadogo, W.R., R. Boly, M. Lompo, N. Some, C.E. Lamien, I.P. Guissou and O.G. Nacoulma, 2006b. Anti-inflammatory, analgesic and antipyretic activities of *Dicliptera verticillata*. Int. J. Pharmacol., 2 (4): 435-438.

Sharma, P.C., M.B. Yelne and T.J. Dennis, 2001. Database on medicinal plants used in Ayurveda. Central Council for Research in Ayurveda and Siddha, Department of Indian system of medicine, Govt. of India, New Delhi, 1: 396, 3: 11, 158, 282, 5: 43, 172, 263.

Shastri, S.N., 1988. Charak Samhita (Sutra Sthanam). Chaukhamba Bharati Academy, Varanasi. 4: 92-93.

Shay, H., S.A. Komarow, S.S. Fels, D. Meranze, M. Gryenstein and H. Siplet, 1945. A simple method for the uniform production of gastric ulceration in rat. Gastroenterology, 48 (5): 43-61.

Simon, L.S., 1995. Actions and toxicity of nonsteroidal anti-inflammatory drugs. Curr. Opin. Rheumatol., 7 (3): 159-166.

Suleyman, H., B. Demircan and Y. Karagoz, 2007. Anti-inflammatory and side effects of cyclooxygenase inhibitors. Pharmacol. Rep., 59: 247-258.

Valsaraj, R., P. Pushpangadan, U.W. Smitt, A. Adsersen, S.B. Christensen, A. Sittie, U. Nyman, C. Nielsen and C.E. Olsen, 1997. New anti- HIV-1, antimalarial and antifungal compounds from *Terminalia belerica*. J. Nat. Prod., 60 (7): 739-742.

Veerappan, A., S. Miyazaki and R. Dhananjayan, 2005. Studies on the anti-inflammatory, antipyretic and analgesic properties of the leaves of *Aegle marmelos*. Corr. J. Ethnopharmacol., 96 (1-2): 159-163.