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Assessment of antinociceptive potentials of two Ayurvedic herbal preparations Balarishta and Sarivadyarishta

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ABSTRACT

Balarishta and Sarivadyarishta are two Ayurvedic herbal formulations used by Ayurvedic practitioners in Bangladesh for treatment of rheumatic pain. The objective of the present study was to evaluate the antinociceptive potentials of these two herbal formulations in acetic acid-induced gastric pain model in Swiss albino mice. When administered orally at doses of 0.3, 1.0, and 1.5 ml per kg body weight, Balarishta caused dose-dependent and significant reductions in the number of abdominal constrictions in mice induced by intraperitoneal administration of acetic acid. At the afore-mentioned three doses, the percent reductions in the number of constrictions were, respectively, 41.4, 44.8, and 55.2. At a dose of 0.1 ml per kg body weight, Balarishta decreased the number of abdominal constrictions by 31.0%, but the result was not statistically significant. In comparison, a standard antinociceptive drug, aspirin, when administered at a dose of 200 mg per kg body weight, decreased the number of abdominal constrictions in acetic acid-induced gastric pain mice by 37.9%. Thus even at a dose of 0.3 ml per kg body weight, Balarishta demonstrated greater potency than aspirin in pain alleviation. A combination of aspirin (200 mg per kg body weight) and Balarishta (1 ml per kg body weight) reduced the number of abdominal constrictions by 58.6%. Sarivadyarishta, when administered orally at doses of 0.1, 0.3, 1.0 and 1.5 ml per kg body weight demonstrated dose-dependent and significant reductions in the number of abdominal constrictions only at the three higher doses. At these three doses, Sarivadyarishta reduced the number of constrictions, respectively, by 48.3, 55.2, and 58.6%. Like Balarishta, the percent reduction in the number of abdominal constrictions with a dose of 0.3 ml Sarivadyarishta per kg body weight was greater than that of aspirin. A combination of aspirin (200 mg per kg body weight) and Sarivadyarishta (1 ml per kg body weight) reduced the number of abdominal constrictions by 62.1%. The results not only validate the use of these two herbal preparations for alleviation of rheumatic pain, but further suggests that the two herbal formulations can be used instead of aspirin, which when taken for long time periods (as in the case of rheumatic patients) can cause gastric ulcerations.

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INTRODUCTION

Ayurveda is possibly the most ancient system of medicine in India with a well-defined formulary and a philosophy which gives an explanation for the occurrence of various diseases. It is considered to have arisen more than 5,000 years ago. Mention of plants for medicinal uses can be found in Rig Veda and Atharva Veda, besides classical Ayurvedic texts like Charaka Samhita and Sushruta Samhita, the latter being written somewhere between 1,000 and 600 BC. The other three texts are much earlier than that. At present, more than 1,200 species of plants, nearly 100 minerals and over 100 animal products comprise the Ayurvedic pharmacopoeia (Sekar and Mariappan, 2008). Ayurvedic medicines include arishtas (fermented decoctions) and asavas (fermented infusions), and these are considered as unique and valuable preparations for treatment (Dhiman, 2004). Two such arishtas, namely, Balarishta and Sarivadyarishta are two Ayurvedic herbal formulations used by Ayurvedic practitioners in Bangladesh for treatment of rheumatic pain.

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We had been conducting ethnomedicinal surveys among the folk and tribal medicinal practitioners of Bangladesh for the last several years (Rahmatullah *et al*., 2009a-c; Rahmatullah *et al*., 2010a-g; Rahmatullah *et al*., 2011a,b; Rahmatullah *et al*., 2012a-d). From the information obtained from the traditional healers, further studies are conducted on selected floral species towards evaluation of their antinociceptive, antihyperglycemic, and cytotoxic potential (Anwar *et al*., 2010; Jahan *et al*., 2010; Khan *et al*., 2010; Mannan *et al*., 2010; Rahman *et al*., 2010; Rahmatullah *et al*., 2010h; Shoha *et al*., 2010; Ali *et al*., 2011; Barman *et al*., 2011; Hossan *et al*., 2011; Jahan *et al*., 2011; Rahman *et al*., 2011; Sutradhar *et al*., 2011; Ahmed *et al*., 2012; Arefin *et al*., 2012; Haque *et al*., 2012; Sathi *et al*., 2012). These studies have recently been extended to include traditional medicines from other traditional medicinal systems from Bangladesh, as well as other countries, to evaluate antinociceptive and antihyperglycemic potential of various herbal products. The objective of the present study was to evaluate the antinociceptive potential of Balarishta and Sarivadyarishta in acetic acid-induced gastric pain model in mice.

MATERIALS AND METHODS

Balarishta and Sarivadyarishta were obtained from Sadhana Oushadhaloy Ltd., Dhaka, Bangladesh, which is one of the oldest Ayurvedic product manufacturers in the country. The contents of Balarishta (liquid preparation), as given on the bottle, were per 5 ml, 1.2 mg of roots of *Sida cordifolia* L. (Malvaceae; Ayurvedic name: Berela), 1.2 mg of *Withania somnifera* (L.) Dunal (Solanaceae; Ayurvedic name: Ashwagondha), 2.4 mg of *Lilium polyphyllum* D. Don. (Liliaceae; Ayurvedic name: Kshir kakoli), and 2.4 mg of *Jatropha gossypifolia* L. (Euphorbiaceae; Ayurvedic name: Eranda). The product was described on the bottle to prevent rheumatism, to decrease fever, and decrease general weakness. The manufacturing license number was given as Ayu-058. Dosage as given on the bottle was 4 teaspoonfuls with equal amount of water to be taken daily. The contents of Sarivadyarishta (liquid preparation), as given on the bottle, were per 5 ml, 0.08g *Ichnocarpus frutescens* R. Br. (Apocynaceae; Ayurvedic name: Shyam lota), 0.08g *Hemidesmus indicus* (L.) W.T. Aiton (Apocynaceae; Ayurvedic name: Ananto mul), and 0.08g *Tinospora cordifolia* (Willd.) Hook.f. & Thomson (Menispermaceae; Ayurvedic name: Guduchi). The product was described on the bottle to treat every form of rheumatism. The manufacturing license number was given as Ayu-058. Dosage as given on the bottle was 2-4 teaspoonfuls with equal amount of water to be taken twice daily after meal.

Chemicals:

Glacial acetic acid was obtained from Sigma Chemicals, USA; aspirin was obtained from Square Pharmaceuticals Ltd., Bangladesh.

Animals:

In the present study, Swiss albino mice (male), which weighed between 22-25 g were used. The animals were obtained from International Centre for Diarrheal Disease Research, Bangladesh (ICDDR,B). All animals were kept under ambient temperature with 12h light followed by a 12h dark cycle. The animals were acclimatized for three days prior to actual experiments. The study was conducted following approval by the Institutional Animal Ethical Committee of University of Development Alternative, Dhaka, Bangladesh.

Antinociceptive activity:

Antinociceptive activity of Balarishta and Sarivadyarishta was examined using previously described procedures (Shanmugasundaram and Venkataraman, 2005). Briefly, mice were divided into twelve groups of five mice each. Group 1 served as control and was administered vehicle only. Group 2 was orally administered the standard antinociceptive drug aspirin at a dose of 200 mg per kg body weight. Groups 3-6 were administered Balarishta at doses of 0.1, 0.3, 1.0, and 1.5 ml per kg body weight, respectively. Group 7 was administered a combination of aspirin and Balarishta at doses of 200 mg and 1.0 ml per kg body weight, respectively. Groups 8-11 were administered Sarivadyarishta at doses of 0.1, 0.3, 1.0, and 1.5 ml per kg body weight, respectively. Group 12 was administered a combination of aspirin and Sarivadyarishta at doses of 200 mg and 1.0 ml per kg body weight, respectively. All mice were individually weighed and dose determined on the basis of individual weight. Following a period of 60 minutes after oral administration of standard drug or extract, all mice were intraperitoneally injected with 1% acetic acid at a dose of 10 ml per kg body weight, which causes abdominal constrictions due to gastric pain from acetic acid. A period of 15 minutes was given to each animal to ensure bio-availability of acetic acid, following which period, the number of abdominal constrictions was counted for 10 min.

Statistical analysis:

Experimental values are expressed as mean ± SEM. Independent Sample t-test was carried out for statistical comparison. Statistical significance was considered to be indicated by a p value < 0.05 in all cases.

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RESULTS AND DISCUSSION

When administered orally at doses of 0.3, 1.0, and 1.5 ml per kg body weight, Balarishta caused dose-dependent and significant reductions in the number of abdominal constrictions in mice induced by intraperitoneal administration of acetic acid. At the afore-mentioned three doses, the percent reductions in the number of constrictions were, respectively, 41.4, 44.8, and 55.2. At a dose of 0.1 ml per kg body weight, Balarishta decreased the number of abdominal constrictions by 31.0%, but the result was not statistically significant. In comparison, a standard antinociceptive drug, aspirin, when administered at a dose of 200 mg per kg body weight, decreased the number of abdominal constrictions in acetic acid-induced gastric pain mice by 37.9%. Thus even at a dose of 0.3 ml per kg body weight, Balarishta demonstrated greater potency than aspirin in pain alleviation. A combination of aspirin (200 mg per kg body weight) and Balarishta (1 ml per kg body weight) reduced the number of abdominal constrictions by 58.6%. Sarivadyarishta, when administered orally at doses of 0.1, 0.3, 1.0 and 1.5 ml per kg body weight demonstrated dose-dependent and significant reductions in the number of abdominal constrictions only at the three higher doses. At these three doses, Sarivadyarishta reduced the number of constrictions, respectively, by 48.3, 55.2, and 58.6%. Like Balarishta, the percent reduction in the number of abdominal constrictions with a dose of 0.3 ml Sarivadyarishta per kg body weight was greater than that of aspirin. A combination of aspirin (200 mg per kg body weight) and Sarivadyarishta (1 ml per kg body weight) reduced the number of abdominal constrictions by 62.1%. The results are shown in Table 1.

The anti-inflammatory effect of Balarishta has been reported against cotton pellet induced granuloma in albino rats (Alam *et al*., 1998). As mentioned before, the formulation consisted of four plants, namely *Sida cordifolia*, *Withania somnifera*, *Lilium polyphyllum*, and *Jatropha gossypifolia*. The analgesic and antiinflammatory activities of *Sida cordifolia* has been reported (Sutradhar *et al*., 2006). Withaferin A is a component isolated and described from the plant, *Withania somnifera*, with analgesic and antipyretic properties (Sabina *et al*., 2009). The plant also reportedly contains beta-sitosterol (Duke, 1992), which may explain its analgesic properties (Santos *et al*., 2011). The use of the Plant, *Lilium polyphyllum*, for rheumatalgia has been reported. The plant is one of the plants among the eight plant combination known as 'Astavarga' plant in Ayurvedic literature (Balkrishna *et al*., 2012). Moreover, one of the chemical components of the plant is linalool, with reported antinociceptive properties (Quintans-Júnior *et al*., 2013). The analgesic and anti-inflammatory activities of *Jatropha gossypifolia* in experimental animal models has also been demonstrated (Panda *et al*., 2009). It can then be expected that the four plants in combination would produce a strong effect in alleviating pain, which has been substantiated in the present study.

The other Ayurvedic formulation tested for antinociceptive activity in the present study was Sarivadyarishta, which contained the plants *Ichnocarpus frutescens*, *Hemidesmus indicus*, and *Tinospora cordifolia*. The anti-inflammatory and analgesic activity of roots of *Ichnocarpus frutescens* has been shown in acute and chronic phase inflammation models in rats (Pandurangan *et al*., 2008). Hydro-alcoholic fraction of *Hemidesmus indicus* root has been shown to give analgesic, antipyretic and anti-inflammatory effect in experimental animals, which included testing for analgesic activity through the acetic acid-induced writhing response (Farook *et al*., 2011). The roots of the plant, besides other constituents, also reportedly contain alpha-amyrin, beta-amyrin and beta-sitosterol (Duke, 1992). Methanol leaf extract of the plant *Ligustrum morrisonense* containing amyrin has been shown to demonstrate analgesic activity in rodents (Wu *et al*., 2011). Both alpha- and beta-amyrin has been shown to inhibit inflammatory and neuropathic persistent pain in mice through activation of cannabinoid receptors (da Silva *et al*., 2011). Methanol extract of stem bark of *Cariniana rubra* containing alpha- and beta-amyrin, and beta-sitosterol reportedly showed antinociceptive effects in acetic acid-induced gastric pain models (Santos *et al*., 2011). Analgesic effect has also been observed with an herbal formulation containing stems of *Tinospora cordifolia* (Gupta *et al*., 2013). Thus, once again, scientific reports indicate that the combination of the three plants can produce together a strong effect in alleviation of pain, which has been validated in the present study.

Ayurvedic formulations are time-tested formulations for they have been used for thousands of years. As more and more researchers are turning towards traditional formulations for discovery of better medicines, scientific validation of Ayurvedic formulations can provide the basis for newer and more effective drugs. Moreover, scientific validations of these formulations can lead to the use of the formulations directly and with confidence. Pain is experienced for a variety of causes by millions of people throughout the world on a daily basis. Moreover, diseases like rheumatism or certain forms of cancer can cause chronic pain, and for which diseases there are only symptomatic cures in allopathic medicine. However, pain killing drugs in allopathic medicine like aspirin or paracetamol can, because of over-dosage or long-term use, cause gastric ulcerations or hepatotoxicity. Ayurvedic formulations can be effective substitutes for allopathic medicines in these types of diseases, provided scientific studies demonstrate that no toxic effects occur with the administration of these formulations. On the other hand, the use of Ayurvedic formulations for thousands of years suggest that the formulations are both effective and may not have serious toxic effects.

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Authors of this study have no financial interest in any of the product(s) or manufacturer(s) mentioned in this article.

Table 1: Antinociceptive effects of Balarishta and Sarivadyarishta in the acetic acid-induced gastric pain model mice.

Treatment	Dose (mg or ml/kg body weight)	Mean number of abdominal constrictions	% inhibition
Control (Group 1)	10 ml	5.8 ± 0.86	-
Aspirin (Group 2)	200 mg	3.6 ± 0.73	37.9*
Balarishta (Group 3)	0.1 ml	4.0 ± 1.05	31.0
Balarishta (Group 4)	0.3 ml	3.4 ± 0.68	41.4*
Balarishta (Group 5)	1.0 ml	3.2 ± 0.83	44.8*
Balarishta (Group 6)	1.5 ml	2.6 ± 0.40	55.2*
Balarishta + Aspirin (Group 7)	1.0 ml + 200 mg	2.4 ± 0.24	58.6*
Sarivadyarishta (Group 8)	0.1 ml	6.0 ± 0.89	-
Sarivadyarishta (Group 9)	0.3 ml	3.0 ± 0.89	48.3*
Sarivadyarishta (Group 10)	1.0 ml	2.6 ± 0.68	55.2*
Sarivadyarishta (Group 11)	1.5 ml	2.4 ± 0.40	58.6*
Sarivadyarishta + Aspirin (Group 12)	1.0 ml + 200 mg	2.2 ± 0.37	62.1*

All administrations (aspirin, Balarishta and Sarivadyarishta) were made orally. Values represented as mean ± SEM, (n=5); *$P < 0.05$; significant compared to control.

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