An Evaluation of Some Medicinal Plants Used To Treat Pain in Bangladesh

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Abstract
Pain is an unpleasant physical and emotional experience, which can be caused by numerous factors and resulting in even traumatic situations. Most commonly, pain is classified as acute or short-term or chronic meaning long-term. While acute pain may cause transient but serious disturbances in a person’s quality of life, chronic pain certainly does so. Medications used to treat pain include non-steroidal anti-inflammatory drugs like ibuprofen, naproxen and aspirin; acetaminophen; anti-depressants; and anti-seizure medications. Since more or less all of these drugs have adverse side-effects, it is necessary to find alternate drugs for alleviating pain. Bangladesh has a long history of folk medicinal practitioners (FMPs), who essentially use medicinal plants for treatment of numerous diseases and symptoms including pain. However, the experience of FMPs is generally transmitted orally from generation to generation and no formal training is necessary for them to practice. As such, it is necessary to perform critical evaluations of the plants that they use, not only to determine any harmful effects, but also to evaluate the potential of any given plant or plant part towards discovery of lead compound and new drugs. In this study we evaluated a number of plants (eight) used by a FMP of Rangpur district, Bangladesh, which plants are used by the FMP to treat various types of pain. The plants were evaluated on the basis of similar ethno medicinal uses in other parts of the world, and on any analgesic activity reports on the plant or photochemical constituent(s) present therein. Surprisingly, despite the apparent lack of scientific training of the FMPs, scientific literature validates most of their claims of analgesic activity in the plants that they use to treat pain. As such, the plants present a distinct potential for discovery of novel analgesic drugs.

Keywords
Analgesic; Antinociceptive; Folk Medicine; Medicinal Plants; Rangpur; Bangladesh

Introduction
Pain can arise from many different causes. Chronic pain is associated with incurable diseases or stress like cancer [1], arthritis [2], herniated lumbar discs [3] or continuous stress [4], while acute pain can be a result of more mundane causes like bumps, cuts, or sprains. Essentially there can be thousands of factors leading to pain, from poor food habits to over-work and stressful conditions in the home or work-place to various diseases. Medications used to treat pain include non-steroidal anti-inflammatory drugs like ibuprofen, naproxen and aspirin; acetaminophen; anti-depressants; and anti-seizure medications. All these drugs have mild to serious adverse effects ranging from gastric discomfort to addiction. As a result, it would be beneficial to discover new analgesic drugs with less adverse effects.

Plants have always proved to be excellent sources for new drugs. This has also included analgesic and anti-inflammatory drugs, obtained from plants like...
The original study was carried out in Rangpur district, Bangladesh (located in between 25°18’ and 25°57’ north latitudes and in between 88°56’ and 89°32’ east longitudes) in 2014. The FMP resided at Palashbari village in the district. A total of 17 plants were obtained from the FMP, out of which 8 plants were used for analgesic purposes. Scientific reports on ethno medicinal studies, phytochemical constituents and pharmacological activities were collected by searching various data bases like Google Scholar, SCOPUS and Pub Med.

For review of the literature (that is scientific reports, particularly ethno medicinal studies), we have chosen mostly the narrative system of review. Although this form of review has some basic weaknesses like there is no rule as to how the primary data was obtained (different studies may follow different methods for obtaining primary data); consequently integration of results from different studies may be difficult. However, in this case, the primary data was obtained by us. Any integration with other studies is not necessary. Nor it is necessary to synthesize quantitatively the mode of collection of information or extent of analysis by other researchers. So long as the information was collected accurately by other researchers is enough to merit incorporation in the references. And we relied on published work to ensure that the information given was most probably accurately collected. Also to be noted is that for our purposes, any published ethno medicinal information in the scientific literature that tallied with our information (like the same plant reported by us was used to treat pain was used similarly in other parts of the world) is good enough to suggest that the plant quite possibly be a source of new drugs. It is to be further noted that as our title indicates, the objective of this study was to determine whether any pharmacological studies in the scientific literature exists on the analgesic properties of the plant that is being reported by us to treat pain in our study area. Our objective was to validate the traditional analgesic use with scientific reports of analgesic properties of a given plant, and so validate traditional uses.

Results and Discussion

The plants and their various analgesic uses are shown in Table 1. A total of 8 plants were used by the FMP to treat body pain, rheumatic pain, and toothache. Except for one formulation containing 2 plants, the rest were mono herbal formulations. The formulations were fairly simple, and consisted of pills or juice obtained from whole plant or plant parts.

In the Discussion part, since this review is about a critical evaluation (that is scientific validation) of plants used by traditional practitioners to alleviate different types of pain, we shall concentrate on pharmacological reports in scientific journals on analgesic and anti-inflammatory properties of the plants used by the traditional practitioners and reports on phytochemicals present in the plants used, which phytochemicals have scientifically reported analgesic and anti-inflammatory properties. Pain and inflammation often go together, and so analgesic and anti-inflammatory properties are both considered. Only those reports have been chosen from the available literature, where the methodology appears to be sound, the experiments well conducted, sample sizes were adequate, and the statistical analysis correctly done (that is appropriate method of statistical analysis was used for interpretation of data and the correct conclusions drawn).
Justicia gendarussa

The use of this plant to treat pain has previously been reported from Bangladesh. The Marma tribal community of Khagrachhari District (located in between 22°38' and 23°44' north latitudes and in between 91°44' and 92°11' east longitudes) uses leaves of the plant to treat waist pain (leaves are boiled in water and massaged onto the waist area) [10]. Leaves are used topically to treat rheumatic pain by the Gor tribe of Sylhet District (located in between 24°36' and 25°11' north latitudes and in between 91°38' and 92°30' east longitudes), Bangladesh [11]. The Pahan tribe of Dinajpur district (located in between 25°10' and 26°04' north latitudes and in between 88°23' and 89°18' east longitudes) use stems of the plant to brush teeth and so avoid toothache [12].

Ethanolic extract of leaves demonstrated analgesic activity in acetic acid-induced writhing and hot plate models in mice [13]. Ethanol extract of aerial parts of the plant also showed anti-inflammatory and analgesic activities [14]. Metabolite profiling of the plant showed presence of friedelin, β-sitosterol, lupeol, apigenin conjugates, and justidrusamides A-D [15]. The anti-inflammatory and analgesic effects of friedelin isolated from Azima tetracantha Lam. has been shown in mice and rat models [16]. The analgesic property of lupeol isolated from Diospyros mespiliformis stem bark has been demonstrated [17]. Lupeol has further been shown to demonstrate analgesic property, which is mediated through the inhibition of IL-1β (interleukin-1beta) and TNF-α (Tumor necrosis factor-alpha) production [18]. Lupeol and ursolic acid have also been demonstrated as the active ingredients responsible for the analgesic and anti-inflammatory activities of methanol extract of Cissus repens in mice [19]. The analgesic activity of β-sitosterol is also well-known [20].

Aristolochia indica and Swertia chirayita

In Ayurveda and Unani systems of traditional medicine in India, the roots of Aristolochia indica are used to treat joint pain [21]. Roots of the plant are administered for abdominal colic by tribals of Mayurbhanj district (the district lies between 21°01'6" and 22°34'6" north latitudes and 85°40'6" and 87°11'6" east longitudes), North Orissa, India [22]. Leaves of Aristolochia indica, Azadirachta indica and Plumbago zeylanica are taken together to treat pain in Manikganj district (located in between 23°38'4" and 24°03'16"

### Table 1: Some Medicinal Plants Used by Folk Medicinal Practitioners of Bangladesh to Treat Pain [9]

<table>
<thead>
<tr>
<th><strong>Scientific Name</strong> (English)</th>
<th><strong>Family Name</strong></th>
<th><strong>Parts used</strong></th>
<th><strong>Reported bio-active phytoconstituents</strong></th>
<th><strong>Disease</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Justicia gendarussa</em> Burm. f. (Willow-leaved Justicia)</td>
<td>Acanthaceae</td>
<td>Whole plant</td>
<td>Friedelin, lupeol, β-sitosterol</td>
<td>Body pain.</td>
</tr>
<tr>
<td><em>Aristolochia indica</em> L. (Indian Birthwort)</td>
<td>Aristolochiaceae</td>
<td>Leaf</td>
<td>(-)-Hinokinin, aristolactam I</td>
<td>Rheumatic pain. Pills prepared from <em>Aristolochia indica</em> and <em>Swertia chirayita</em> are orally taken.</td>
</tr>
<tr>
<td><em>Ipomoea mauritiana</em> Jacq. (Giant potato)</td>
<td>Convolvulaceae</td>
<td>Seed</td>
<td>Hexadecen-1-ol trans 9, hexadecanoic acid</td>
<td>Rheumatic pain.</td>
</tr>
<tr>
<td><em>Derris indica</em> (Lamk.) Bennet (Indian beech)</td>
<td>Fabaceae</td>
<td>Fruit</td>
<td>No reports available</td>
<td>Rheumatic pain.</td>
</tr>
<tr>
<td><em>Mimosa pudica</em> L. (Touch me not)</td>
<td>Fabaceae</td>
<td>Root</td>
<td>β-Sitosterol, quer cetin</td>
<td>Toothache.</td>
</tr>
<tr>
<td><em>Swertia chirayita</em> (Roxb. ex Fleming.) H.Karst. (Chirayita)</td>
<td>Gentianaceae</td>
<td>Leaf</td>
<td>Gentianine, swertiamarin</td>
<td>See <em>Aristolochia indica</em>.</td>
</tr>
<tr>
<td><em>Vitex trifolia</em> L. f. (Simpleleaf chastetree)</td>
<td>Verbenaceae</td>
<td>Leaf, stem</td>
<td>Luteolin, ursolic acid, vitexin</td>
<td>Body pain, pain due to injury, joint pain. Toothache, swelling of gums, bleeding from gums, loosening of teeth.</td>
</tr>
</tbody>
</table>
north latitudes and in between 89°41' and 90°08’ east longitudes), Bangladesh [23].

Since Aristolochia indica was used by the FMP against rheumatic pain, it is possible that the plant acted as an anti-inflammatory agent and through reducing rheumatism-induced inflammation also reduced pain. Interestingly, some compounds isolated from the plant include astragalin, (-) hinokinin, aristolactam I, and aristolochic acids I and II; among these compounds, (-) hinokinin and aristolactam I showed anti-inflammatory potential [24].

The plant was used by the FMP in combination with Swertia chirayita. Dried whole plants are used by the Monpa tribe from the Zemithang (27.71° north and 91.73° east) Region, Arunachal Pradesh, India, to treat malaria, a diseases characterized by a high degree of body pain [25]. The plant is used to cure stomach ache by the Lepcha tribe of Dzongu valley (27.51° north, 88.4375° east) in North Sikkim, India [26]. Ethanolic root extract has been shown to demonstrate both analgesic and anti-inflammatory activities [27]. Methanolic extract of whole plant showed analgesic activity in mice and rats using hotplate and tail flick methods [28]. Among the various phytochemicals reported to be present in the plant, gentianine has anti-inflammatory properties; swertiamarin has pain-relieving properties [29, 30]. Thus the two plants in combination may be more effective in alleviating pain and inflammation. Also interestingly, sub-chronic toxicity of liver and kidney functions has been observed with alcoholic extract of aerial parts of Aristolochia indica [31]. On the other hand, the hepatoprotective properties of Swertia chirayita have been described [32]. The plant also has uses against kidney diseases [33].

Calotropis gigantea

The plant, particularly the leaves have widespread ethnic uses for treatment of pain. Leaves are used to treat joint pain in Narayanganj district (located in between 23°33’ and 23°57’ north latitudes and in between 90°26’ and 90°45’ east longitudes), Bangladesh [34]. Leaves are used to treat body pain in Pabna district (located in between 23°48’ and 24°21’ north latitudes and in between 89°00’ and 89°44’ east longitudes), Bangladesh [35]. Leaves are also used to treat body pain in Dinajpur district (located in between 25°10’ and 26°04’ north latitudes and in between 88°23’ and 89°18’ east longitudes), Bangladesh [36]. The Bede community of Porabari village in Dhaka district (located in between 23°53’ and 24°06’ north latitudes and in between 90°01’ and 90°37’ east longitudes), Bangladesh has eight formulations containing the plant to treat rheumatic pain [37]. The Bhil tribe of Bibdod, Madhya Pradesh (22.97° north, 78.66° east), India, uses the latex of leaves to treat back pain [38]. Leaves soaked in castor oil and heated are used to treat pain arising from rheumatoid arthritis by tribes of Pipikondalu Forest, Andhra Pradesh (15.91° north, 79.74° east), India [39].

Analgesic activity of the plant along with phytochemical constituents of various parts has been reviewed. The leaves reportedly contain calotropagenin, calactin, calotoxin, calotropin, taraxaxeryl acetate, β-sitosterol, stigmasterol α- and β-amyrin. Analgesic activity of dry latex has been shown [40]. Analgesic and anti-inflammatory activities has been shown for Ethanolic leaf extract using formalin-induced paw lick and carrageenan-induced paw edema in rats and acetic acid-induced writhing models in mice [41]. The analgesic activity of β-sitosterol has been reviewed [42]. Hexane extract of leaves of Buddleja globosa, which showed analgesic activity, was found to contain α- and β-amyrins, -sitosterol, stigmasterol, stigmastenol, stigmastanol and campesterol [43]. The analgesic and anti-inflammatory activities of α- and β-amyrin from Protium heptaphyllum as demonstrated through writhing and formalin tests in mice are known [44].

Ipomoea mauritiana

In Jhalokati district, Bangladesh, FMPs use the plant to treat pain in bones and gastric pain [45]. The Nag clan of the Rai Ghatual tribe in Moulibazar district (located in between 24°08’ and 24°29’ north latitudes and in between 91°36’ and 92°17’ east longitudes), Bangladesh use rhizomes to treat stomach ache [46]. Callus extract of Ipomoea mauritina showed analgesic activity in acetic acid-induced writhing model in mice [47]. Bio-active constituents reported from the tuber include hexadecen-1-ol trans 9 and hexadecanoic acid with anti-inflammatory properties and activities [48].

Derris indica

There are no reports on pharmacological activity studies or phytochemical constituents of the plant. Also apart from one [9], there are also no ethnomedicinal reports (to the best of our knowledge). However, analgesic activity of leaves of another Derris species, Derris trifoliata has been reported [49].
Mimosa pudica

The plant is traditionally used for arthritis in Chhattisgarh State, India [50]. The plant is used against caries by Malayali tribals of Kolli Hills (11.25° north, 78.34° east), India [51]. The plant is used in Mexico and Nicaragua for stomach pain, and in Panama to treat headache [52].

The antinociceptive activity of aqueous extract of the whole plant in acetic acid-induced writhing test and hot plate test has been reported [53]. Hot plate, tail flick, acetic acid-induced writhing test and carrageenan-induced paw edema tests demonstrated analgesic and anti-inflammatory activities of the Ethanolic extract of whole plant [54, 55].

The plant is known to contain mimosine, β-sitosterol, stigmasterol, leucoanthocyanidin, dimethyl crocetin, quercetin and luteolin derivatives, mimosainic acid, and mimosinamine [55, 56]. Beta-sitosterol is a known analgesic compound [42]. Quercetin has been observed to reduce Ehrlich tumor-induced cancer pain in mice [57].

Vitex trifolia

Fruits of this plant are known to be used for curing headache, migraine, and rheumatism in Asian countries [58-60]. Leaves are known to contain flavones glycosides, luteolin, ursolic acid, and m-hydroxy benzoic acid, and flavonoids such as casticin, vitexin, artemetin, coniferaldehyde and vanillin [61]. Luteolin, ursolic acid and vitexin are known analgesic or anti-inflammatory agents [62-65]. The analgesic potential of the plant has been demonstrated in acetic acid-induced writhing test in mice and tail immersion methods in rats [66].

The structures are given in Figure 1 for several relevant bio-active constituents with analgesic or anti-inflammatory activities. Photographs of three plants as mentioned in the text are shown in Figures 2-4.

**Figure 1**: Some of the Phytochemicals with Reported Analgesic or Anti-Inflammatory Properties
Conclusions

A perusal of the scientific literature on ethnomedicinal use reports, phytochemical constituents, and pharmacological activity reports on the plants used by a FMP of Rangpur district in Bangladesh to alleviate various types of pain showed that the plants are scientifically validated in their traditional uses and as such, can be effective sources of new drugs against pain, which may be more affordable to the poorer segments of the population. If potential new drugs from these plants have less or no adverse effects versus existing drugs, that would provide additional benefit. Plants have always been a source for lead compounds, and many modern drugs like reserpine, quinine, vincristine, and vinblastine, to name only a few, has been discovered from close observations of traditional medicinal practices of indigenous peoples. The positive correlation between analgesic uses of the plants by the FMP and scientific reports on the analgesic activities of the plants as demonstrated in scientific studies suggest that once again the ethnic uses may prove to be important clues in discovery of pain alleviating drug(s) or lead compounds from the plants.

Since this is not an extensive ethnomedicinal review of the plants used by the Bangladesh FMP for treatment of pain, we have limited ourselves to mostly ethnomedicinal literature of Bangladesh and neighboring India describing the uses of these plants for alleviating pain. It is quite possible that other reports may be found in the literature about the use of these plants for pain alleviation from other ‘hot spots’ of the world like Brazil or Indonesia, but in our opinion that is beyond the scope of the present review. The objective of this review has been to analyze the use of some plants by a FMP from Bangladesh for alleviating pain with reference to scientific reports on the analgesic activities of the same plants, and the comparison clearly shows that the traditional analgesic uses appear to be validated by science. Nevertheless, it is expected that this review will spur more scientific interest in these plants leading to isolation and identification of relevant bio-active compounds and toxicity studies on the compound(s) of interest leading to possible discovery of lead compounds and new drugs.

Declarations

The authors declare that they have no conflicts of interest.
References


Ethnomed 4: 22.


