A Pharmacological Review of Four Widely Used Traditional Medicinal Plants for Wound Healing in Bangladesh

Md. Rajdoula Rafe1,*, Rayhanus Salam2, Syeda Naureen Ahmed3, Zebunnesa Ahmed2, and Surid Mohammad Chowdhury2

1Department of Pharmacy, Jagannath University, Dhaka-1100, Bangladesh; 2Department of Pharmacy, Southeast University, Dhaka-1213, Bangladesh; 3Department of Pharmacy, Independent University Bangladesh, Dhaka-1229, Bangladesh

Abstract: Traditional and folklore medicines have gained popularity throughout the world due to their safety. Herbal medicines with pharmacological activities and nutritional value are the most popular choice. Cultural and geographical factors of Bangladesh make it a vast source for herbal medicines. In addition, the cost-effectiveness of herbal medicines has also played an important role to make it a drug of choice among the developing countries like Bangladesh. People of Bangladesh have been using plants for centuries to treat different wounds caused by excision and incision. In this current review, we have gone through an extensive literature search to find out the four most commonly used medicinal plants for the treatment of wounds and their pharmacological activities in scientific researches. The featured plants of this review articles are, Calotropis gigantea, Cynodon dactylon, Acorus calamus and Justicia gendarussa. In traditional and herbal medicines, many plants are used without their scientific validation and we intend to perform a literature review in order to find out the potential scientific value of the featured plants. In addition, with pharmacological activities, their traditional formulation as a wound healing drug is also added to this article. This study will help validate the uses of these plants as traditional medicine and for researchers to find out potential therapeutic drugs according to their pharmacological studies.

Keywords: Herbal medicine, wound, pharmacological, formulation, green environment, potential therapeutic drugs.

1. INTRODUCTION

Plants are the most popular sources for discovering and developing novel therapeutic agents. Hence, it is impossible to measure the importance of medicinal plants in human livelihood due to their inseparable contribution to the human life so far [1]. Bangladesh is well known for its green environment enriched with diverse plants. Majority of the Bangladeshi population lives in the rural area, and the rural and tribal group rely greatly on traditional medicines derived from plants [2]. For centuries, Bangladeshis have used a traditional approach to treat ailments. Traditional and folk medicine systems of Bangladesh depend substantially on plant sources as different parts of a plant can be used to treat different diseases [3]. The practice of using the traditional system of medicines as well as the knowledge of treatment systems is passed from one generation to another [4-7].

In recent years, the potentiality and availability of traditionally used medicinal plants have made it an exciting topic for researchers [8]. Currently, the
most critical aspects of discovering an effective therapeutic agent include having fewer side effects and adverse effects and for these parameters, folklore and traditional medicine make itself a valuable source [9]. Based on the various therapeutic effects of plants, numerous researches have been carried out on ethnomedicines [10]. Through the traditional medicine system, plants have been used for a long time to heal various types of wounds [11]. Healthcare resources are now utilizing a considerable amount of economy for the treatment of chronic wounds [12].

A number of studies revealed that a significant gap exists between scientific validation of ethnomedicine and their uses [13]. In this review article, we collected information about four plants with wound healing activities that are used as traditional medicines in Bangladesh. Also the pharmacological activities of the plants have been reviewed from various reputed scientific journals in order to find a relation between the conventional use and pharmacological effects of the plants. This review may help scientists and researchers working in complementary and alternative medicine to find out a possible biologically active compound by analyzing it chemically and explore the modern health sector. This review also covers the traditional formulations of plants, which are still used to treat wounds.

2. TRADITIONAL USES FOR WOUND HEALING MEDICINE

The traditional forms of using plants to heal wound involve the use of similar plants as a topical agent in the wounded area like poultice made with crushed plants or from the juice of the plants [14]. Shoot, leaves, barks, fruits, stems, flower and even whole plants can be used to make a formulation. In majority of the cases, plants are used without any solvent systems although sometimes a little amount of water can be used.

After a broad literature search, the most common formulations that we found for our featured plants are given below in Table 1.

3. PHARMACOLOGICAL ACTIVITIES

3.1. Pharmacological Studies of Calotropis gigantea

3.1.1. Wound Healing Effects

In a study, the latex extracts of Calotropis gigantea have shown significant wound healing activity against the wounds of albino mice model with excision and incision wounds. In this experiment, the dose of 200 mg/kg/day of plant extracts showed an 83.2% reduction of the wound area, whereas the control group showed a 76.22% reduction [15]. C. gigantea can also be used as a topical preparation which can increase the contraction of wounded muscles significantly. Furthermore, topical use of C. gigantea in both excision and incision model decreased the epithelization time and scar area and increased hydroxyproline were also observed [16].

3.1.2. Antimicrobial Effects

Different extracts of C. gigantea leaves have been reported to have significant activity against

<table>
<thead>
<tr>
<th>Plants Name</th>
<th>Family</th>
<th>Bengali Name</th>
<th>Parts Used</th>
<th>Formulation Used in Local Areas of Bangladesh</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calotropis gigantea</td>
<td>Asclepiadaceae</td>
<td>Akanda</td>
<td>Shoot, whole plant</td>
<td>Crushed shoots of Calotropis gigantea, leaves of Datura metel, flowers of Acacia farnesiana, clove of Allium sativum, and seeds of Brassica campestris are boiled together to make a cake which is used as a poultice to the wounded area [15]</td>
</tr>
<tr>
<td>Cynodon dactylon</td>
<td>Poaceae</td>
<td>Durba ghas</td>
<td>Shoot, Whole plant</td>
<td>This grass type whole plant or the shoots of the plant are chewed to make paste and applied to the wounded area to stop bleeding [16]</td>
</tr>
<tr>
<td>Acorus calamus</td>
<td>Acoraceae</td>
<td>Vojo</td>
<td>Leaf</td>
<td>Crushed leaf is applied to wound [15]</td>
</tr>
<tr>
<td>Justicia gendarussa</td>
<td>Acanthaceae</td>
<td>Bishollo koroni, Bish jaron</td>
<td>Leaf</td>
<td>Crushed leaves are applied as poultice to stop bleeding from external cuts and wounds [15]</td>
</tr>
</tbody>
</table>
Various Candidas like *Candida albicans*, *C. parapsilosis*, *C. tropicalis* and *C. krusei* [17]. A study published by Alam *et al.* claimed that chloroform and methanol fractions of root bark extracts of *C. gigantea* showed potential activity against *Sarcina lutea*, *Bacillus megaterium* and *Pseudomonas aeruginosa* and this same study also claimed that petroleum ether also has a significant activity against *Bacillus subtilis* and *Shigella sonnei* [18].

### 3.1.3. Cytotoxic Effects

Three different doses, 50, 100 and 200 mg/kg body weight were used against the mice model with ascites carcinoma, and the doses were prepared with ethyl acetate extracts of *Calotropis gigantea* flower. Significant decreases in tumor cells and body weight were observed with prolonged survival time. Among these three doses, doses at 200 mg/kg body weight reported maximum activity against tumor cells [19]. Calotropone (1) is a compound isolated from *C. gigantea* plant extracts that exhibited inhibitory effects against cancer cell lines [20]. Another study also reported that calotropin (2), frugoside (3), and 4’-O-β-D-glucopyranosyl-frugoside (4) are the three cardenolides isolated from *C. gigantea* that showed similar cytotoxic activity like cardiac glycoside such as digoxin against cancer cell lines [21]. The structures of these bioactive compounds are given in Fig. (1).

### 3.1.4. Hepatoprotective Activity

Hepatoprotective activity of *Calotropis gigantea* stems extracts was evaluated in Wistar rats with *CCl₄* (Carbon tetrachloride) induced liver damage. In the study, 2 ml/kg body weight dose was used twice a week to observe the activity, and all of the activities were compared with standard silymarin. The hepatoprotective effect was evaluated by estimating various biochemical parameters of plant extracts treated with rat blood and serum and those parameters were aspartate aminotransferase, glutathione, superoxide dismutase, glutathione peroxidase, lipid peroxidase and catalase. In this study, rats treated with plant extracts showed significant hepatoprotective activity compared to the control group [22]. In another study by Agar *et al.*, it was claimed that plant extracts in rats with induced hepatic damage showed protection against serum enzyme levels [23].

### 3.1.5. Hypoglycemic Effect

Glucose pretreated mice model was used to measure hypoglycemic effects of *Calotropis gigantea* methanolic leaf extract. A significant reduction of glucose level was observed after treating at the doses of 100, 200 and 400 mg/kg body weight. Among these three doses, 400 mg/kg body weight showed the maximum reduction in blood glucose of mice with 28.54% reduction [24], whereas the leaves and flower extracts of *C. gigantea* also reduced glucose levels in normal rats. A significant reduction was observed in streptozocin-treated mice after the administration of *C. gigantea* leaves and flower extracts [25].

### 3.1.6. Miscellaneous

Several studies of *Calotropis gigantea* have also reported its potential antipyretic, analgesic, anti-convulsant, anxiolytic, sedative, larvicidal, anti-inflammatory and anti-diarrhoeal activities [26-31].

### 3.2. Pharmacological Studies of *Cynodon dactylon*

#### 3.2.1. Antimicrobial Effects

Rahman reported that aqueous extracts of *Cynodon dactylon* have shown significant activity against both gram-negative and gram-positive bacteria, but methanol extract did not show any specific zone of inhibition [32]. *C. dactylon* crude extract was tested against Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) and the crude extract showed replication inhibitory activity of PRRSV without any cytotoxicity, at the dose of 0.78 mg/ml [33]. At the concentration of 50 µg/ml, luteolin (5) and apigenin (6) fractions (Fig. 1) extracted from *C. dactylon* gave potential antiviral activity [34].

#### 3.2.2. Analgesic and Anti-inflammatory Effects

*Cynodon dactylon* plant ethanol extract of the aerial part has shown significant analgesic activity in 1.2% acetic acid pretreated mice. This ethanol extract also increased analgesic activity in mice treated with morphine and pethidine [35]. Three doses of strength 200, 400, and 600 mg/kg were prepared in order to evaluate the anti-inflammatory activity and all of these doses exhibited potential anti-inflammatory activity in rat paw edema induced by serotonin, carrageenan, dextran, and histamine [36]. Another study also reported the anti-inflammatory
activity of *C. dactylon* plant extract in rats with carrageenan-induced paw edema [37].

### 3.2.3. Wound Healing Properties

The hydroalcoholic fraction of *Cynodon dactylon* plant extracts was evaluated for its wound healing activity in the excision wound rats model. Wound contraction rate and epithelization period were observed. Topical application of 7.5% and 10% plant extracts has shown significant wound healing activity in comparison with standard cephaladine in a rat model [38]. Dande and Khan have also reported significant wound healing activity of aqueous and alcoholic plant extract of *C. dactylon*...
in excision (p < 0.05) and incision (p < 0.01) wound model [39]. In another study, flavonoid-rich extract of *C. dactylon* also improved healing process by significantly increasing collagen protein and decreasing lipid peroxide in the wounded area [40].

### 3.2.4. Effects on CNS

The pentylenetetrazole-induced animal model was used to evaluate the effects of convulsion of ethanol extract of *Cynodon dactylon* plant. The plant extract significantly inhibited the convulsion, and inhibitory effect increased with the increasing dose of the extracts [35]. Also convulsion of mice induced by convulsive agents decreased by ethanol extracts of aerial parts of *C. dactylon* plants. In a mice model, the anticonvulsive effect exhibited changes in amino acids and catecholamine levels of the brain [41].

### 3.2.5. Anti-diabetic Activity

After treating a diabetic mice model with *Cynodon dactylon* aqueous plant extract at three different doses (250, 500 and 1000 mg/kg body weight), 500 mg/kg body weight dose showed the most significant activity of lowering of blood glucose level by 31% [42, 43]. Furthermore, the ethanol extract of *C. dactylon* root stalks has been reported to exhibit potential anti-diabetic activity [44]. Another study by Jarald *et al.* also suggested wound healing activities of *A. calamus* leaves [50].

### 3.2.6. Miscellaneous

The various types of extracts with different parts of the plant *C. dactylon* show antioxidant, hypolipidemic [42], immunomodulatory, hepatic antioxidant [46] and cardioprotective [47] activities.

### 3.3. Pharmacological Studies of *Acorus calamus*

#### 3.3.1. Wound Healing Activity

After analyzing the wound healing activity of the ethanolic extract of *Acorus calamus* leaves on a rat model with induced incision and excision wound, it was observed that the rat treated with plant extract had significantly increased tensile strength of granulation tissue with a decrease in the period of epithelialization compared to the control group [48]. Topical administration of aqueous *A. calamus* plant extract exhibited potential skin wound healing properties and *in vitro* anti-inflammatory activity by inhibiting mRNA expressions of inflammatory cells [49]. Another report by Ponrasu *et al.* also suggested wound healing activities of *A. calamus* leaves [50].

#### 3.3.2. Insecticidal Effect

The insecticidal effect of essential oil vapors of *Acorus calamus* rhizomes was evaluated on several insects, and the vapors showed toxic effects on *Callosobruchus chinensis*, *Sitophilus granarius*, *Sitophilus oryzae*, *Tribolium confusum* and *Rhyzopertha dominica* [51]. The vapor of essential oil of *A. calamus* was exposed to adult insects as well as to the eggs and a reduction of oviposition was observed in a dose-dependent manner [52]. Liu *et al.* suggested that the essential oil of *A. calamus* and its other constituents can be used to develop natural insecticides [53].

#### 3.3.3. Antimicrobial Activity

After fractionation of the crude methanol extract of *A. calamus* by column chromatography, one of the fractions was examined on some bacteria, yeasts, and fungi, and amongst them, the plant extract showed maximum activity against filamentous fungus [54]. Another study reported that among four fractions (petroleum ether, hexane, chloroform and ethyl acetate) of *A. calamus* leaf and rhizome extracts against fungi, ethyl acetate fraction showed maximum activity [55].

#### 3.3.4. Antioxidant Activity

A study report revealed that the leaf extract of *Acorus calamus* contained higher amounts of phenolics, flavonoids, and proanthocyanidins than the rhizome extract. On the other hand, leaf extract showed 2, 2-diphenyl-1-picrylhydrazyl (DPPH) free radical-scavenging, ferrous ions chelating and reducing power activities, whereas *A. calamus* rhizome extracts exhibited scavenging activity against superoxide anion [56]. Acuña *et al.* also reported that ethyl acetate extracts of *A. calamus* showed potent free radical scavenging activity [57]. Another report claimed that at a concentration of 0.2 g/ml, the plant extract exhibited 86.3% inhibitory activity in DPPH scavenging activity [58].

#### 3.3.5. Activity on CNS

Volatile oil isolated from *Acorus calamus* plant extracts indicated protective activity against elec-
trically induced convulsions [59]. Asarone (7), a compound (Fig. 1) extracted from *A. calamus* showed protective activity against metrazol-induced and electrically-induced shock in rats, but not in picrotoxin-induced convulsions [60, 61]. In another study it was reported that the ethanol extract of *A. calamus* rhizomes exhibited different effects in different behavioral tests [62].

3.3.6. Miscellaneous

Several other studies on this plant have reported other activities such as analgesic activity [63], anti-mutagenic activity [64], anti-asthmatic [65], antispasmodic activity [66], anti-diarrhoeal activity [67] and anticancer activity [68].

3.4. Pharmacological Studies of *Justicia gendarussa*

3.4.1. Anti-arthritic Activity

*Justicia gendarussa* leaves extract has been reported to have potential activity against adjuvant and collagen-induced arthritic rats [69, 70]. Varma *et al.* have reported anti-inflammatory and anti-arthritic activity after conducting *in vitro* studies [71]. The plant extract as well as compounds isolated from *J. gendarussa* leaves and roots exhibited inhibitory effects on trypsin and protein denaturation which indicate the possibility of anti-arthritic activities [72].

3.4.2. Anti-inflammatory Effects

The ethyl acetate fractions of *Justicia gendarussa* root extracts have shown activity against carrageenan-induced paw edema on a rat model that supports the traditional use of this plant [73]. Shikha *et al.* reported in an extensive study on mice that *J. gendarussa* leaves extract have a significant anti-inflammatory as well as analgesic activity in comparison with standard drugs [74].

3.4.3. Antimicrobial Activity

Subramanian *et al.* evaluated the antimicrobial activity of ethanolic and aqueous extracts of leaves and stems of *Justicia gendarussa* on 12 different pathogens. After extensive study, it was revealed that ethanolic and aqueous stem extracts have an inhibitory activity against all experimented pathogens, whereas only ethanolic leaf extract showed slight activity against some pathogens [75]. In another study, chloroform extracts of *J. gendarussa* showed moderate antimicrobial activity with maximum 13.00 nm zone of inhibition [76].

3.4.4. Cytotoxic Activity

Methanolic leaves extract and two flavonoids (Fig. 1) compounds (naringenin (8) and kaempferol (9)) isolated from *Justicia gendarussa* were assessed for potential cytotoxic activities against human cancer cell lines, and study result suggested that compounds and methanolic extracts both had significant cytotoxic activities on cancer cell lines [77]. In another study, cytotoxicity of fractionated extract and 70% ethanolic extracts of *J. gendarussa* was observed in cancer cells and it was concluded that both of them were non-toxic to cancer cells [78].

3.4.5. Sedative-hypnotic Effects

In the Indian subcontinent, *Justicia gendarussa* is being used traditionally as a mood-elevating component for a long time. However, a study report suggested that ethanolic plant extract of *Justicia gendarussa* has potential sedative-hypnotic activity compared to the standard Diazepam and this activity was observed in mice model which also revealed that the activity was dependent on the dose of the extract [79].

3.4.6. Miscellaneous

Other reported studies also revealed the corrosive inhibition [80], analgesic [81], hepatoprotective, antioxidants [82], anti-angiogenic [83], and anti-nociceptive activities of *J. gendarussa* plant extracts.

CONCLUSION

Extensive literature study results revealed that the featured plants in this article have potential pharmacological activities against the wound and other related activities like anti-inflammatory and analgesic activities. Although direct scientific research of *Justicia gendarussa* against wound healing was not found, its potential activity against arthritis and inflammation was revealed. Plant sources have been used for a long time to explore medicinal sectors because of their fewer side effects and more effectiveness. Since the featured plants in this literature study are significantly active against various disease conditions, chemical
investigations are needed to find out future lead compounds to develop drugs.

**AUTHOR CONTRIBUTIONS**

All the authors have accepted responsibility for the entire content of this submitted manuscript and approved the submission.

**CONSENT FOR PUBLICATION**

Not applicable.

**FUNDING**

None.

**CONFLICT OF INTEREST**

The authors declare no conflict of interest, financial or otherwise.

**ACKNOWLEDGEMENTS**

Declared none.

**REFERENCES**

[PMID: 9549894]
[http://dx.doi.org/10.1248/cpb.46.528]

[PMID: 19304561]


[http://dx.doi.org/10.1001/omj.2011.26]
[PMID: 22043394]

[http://dx.doi.org/10.1016/j.fitote.2006.09.023]
[PMID: 17113726]

[http://dx.doi.org/10.1016/j.jep.2005.12.024] [PMID: 16446065]

[PMID: 17203820]

[PMID: 15144737]


[http://dx.doi.org/10.1016/S1995-7645(14)60343-6] [PMID: 26005593]

[PMID: 18536171]

[http://dx.doi.org/10.3923/ijp.2011.370.375]


[http://dx.doi.org/10.1111/j.1745-4519.2009.00265.x]

[http://dx.doi.org/10.1016/j.jep.2007.07.039] [PMID: 17889469]


Widely Used Traditional Medicinal Plants for Wound Healing


Current Traditional Medicine, 2020, Vol. 6, No. 1


