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EFFECT OF SELECTED YORUBA MEDICINAL FORMULATIONS ON HEPATIC ARCHITECTURE AND FUNCTIONALITY IN WISTAR ALBINO RATS

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ABSTRACT

This study was undertaken to investigate the effect of Yoruba medicinal formulations on the architecture and structural integrity of hepatocytes and the concomitant effect on its functionality. The Yoruba medicinal formulation derived from plant extract was purchased from a traditional healer at Rumuosi, River state. Healthy albino rats were grouped into three groups, group 1 served as control while group 2 and 3 served as experimental groups. Group 1 received 5% normal saline while group 2 received 2.9µl/kg body weight of the formulation and group 3 received 5.5µl/kg body weight of same formulation. Administration of formulation to both control and experimental groups ran for six weeks during which assay of AST, ALT, ALP, Total Protein, Urea, Bilirubin and creatinine were done at two weeks intervals. Also histological examination of liver was also performed. An increase in the level of AST, ALT and ALP was observed as time increased and also as dosage increased. This coupled with the findings of histological examinations, served as a yardstick for changes in liver architecture. Increase in serum concentration of Bilirubin and decrease in serum concentration of total protein, albumin and urea served as basis for measuring the decreased functionality of the liver. This finding suggests that for lower body weight, hepatotoxicity sets in as a result of the medicinal formulation while for higher body weight, hepatotoxicity can be developed. Despite the many beneficial medicinal advantages of this formulation, their prolonged/long term use results in hepatic damages at the dosage used in this study and thus its use in folkloric medicine should be with uttermost care.

KEYWORDS: Yoruba medicinal formulations, Hepato-toxicity

Cite this article:

INTRODUCTION

Plants and animals are interrelated in their environment. Plants serve as sources of food and medicinal herbs for man and other animals in their environment. For thousands of years, man has depended on plants in order to provide solutions to the myriad of health problems plaguing him (Oliver, 1960).

In the last 20 years, the interest in medicinal plants has increased together with the number of investigations into their biological effects on human beings and animals (Veiga et al., 2005). Although, poisonous plants are ubiquitous, herbal medicine formulations are used by up to 80% of the population in the developing countries (Jaouad et al., 2004). Medicinal plants are believed to be an important source of new chemical substances with potential therapeutic effects (Farnsworth, 1989; Eisner, 1990).

However, despite the numerous reports of the potential beneficial therapeutic effects of Yoruba medicinal formulations derived from plant extract, there have been some adverse effects (Bradie & Gill, 1990, Atawodi et al., 1995; Akinloye et al., 2000).

This study will help to investigate the possible adverse effects of prolonged administration of these Yoruba formulations peddled around our communities on the liver of wistar albino rats.

Herbal medicinal formulation dispensers and patrons have implied that Yoruba medicinal formulations derived from plant extract are unlikely to pose a significant threat to human health; nonetheless, it is important to validate their safety. The confidence in herbal medicines is backed by their long term usage but validation of their safety is necessary because crude herbal medicines are given in most cases without accurate dosage and over ingestion can result in toxicity. It is also possible for the plant to have silent toxic effect that may not be evident within a short time (Mac, 2002). The use of herbal medicinal products may present potential risk to human health (De Smet, 1995), but some toxic herbal medicines have been proven to have beneficial effects at very low doses. Toxic and potent, useful herbal medicines from potentially hazardous plant species include; Digitalis, Nux Vomica (Strychnos), Aconite, Croton Seed, Rauwolfia, Areca, Rotalaria, Dryopteris and Strophanthus. Recent research has revealed that the adverse reactions to herbal products are under-reported (Barnes, 1998). The extensive traditional use of plants as medicines has not enabled herbal medicines with acute and obvious signs of toxicity to be well recognized and their use avoided. However, the report that traditional use of a plant for perhaps many hundreds of years establishes its safety does not necessarily hold true (De Smet, 1995, 1997).

The more subtle and chronic forms of toxicity, such as carcinogenicity, mutagenicity, and hepatotoxicity, may well have been overlooked by previous generations and it is these types of toxicity that are of most concern when assessing the safety of herbal remedies (Shaw, 1995). Limited toxicological data are available on these Yoruba medicinal formulations.

MATERIALS AND METHODS

Formulations:

The Yoruba medicinal formulation derived from plant extract was purchased from a local traditional healer peddling them at Rumuoisi/Rumuekini in Rivers state, Nigeria. The formulation purchased, was one used mainly in treatment of malaria, fever, body and waist pains, typhoid, pile (Jedi-Jedi) and several miscellaneous illnesses and this was confirmed by several patrons in the rural population. The major constituents of the formulation are shown in the table below.
The various plant constituents were purchased alongside the formulation and these plants were identified by the Department of plant science and biotechnology.

Animal treatment:

Healthy wistar albino rats weighing between 125–175g were purchased from the Department of Biochemistry animal house, University of Nigeria Enugu campus, Nigeria.

They were placed in cages (seven in number) kept in a well aerated room at a temperature of 28–31°C and humidity of 50–55%. They were then allowed to acclimatize to new housing conditions for twelve days prior to experimentation. They were feed normal feed (purchased from Top feed shop, Choba) and distilled water *ad libitum.* The cages were cleaned of waste once daily.

Each animal was treated in a manner that complied with the National Institutes of Health (NIH) Guidelines for the Care and Use of Laboratory Animals (N.I.H publication, 1985).

The rats were divided into three (3) groups (groups 1–3). Group 2 and 3 was split into three cages, housed in griffin and George modular cage system. Group 1 served as control group and was fed normal feed and distilled water *ad libitum.* Groups 2 and 3 were fed normal feed and distilled water *ad libitum* and also received the Yoruba medicinal formulation at 2.9 µl/kg body weight and 5.5 µl/kg body weight. The experimental and control groups ran for six weeks post acclimatization, while analysis was carried out every two weeks. At the end of week 4 of experimentation, administration of the formulation was discontinued while the experimentation continued for an extra 2 weeks to serve as a second control, to see the effect after withdrawal.

Sample collection:

Blood:

Each animal was sacrificed by anaesthetizing with chloroform first, then the jugular veins were slit with the aid of a surgical blade. Blood samples for analysis were collected in plane wash bottles.

Organs:

Each animal was laid on a flat hard surface with the fore and hind limbs, pinned to the surface. Their livers were collected after dissection of the underlying skin of the abdominal and thoracic cavities. The samples organs were collected by hand to prevent scaring of the liver tissues by other materials and weighed. Each liver was stored in 10% formalin (BDH) in preparation for histological examination.

Samples were analyzed at the University of Port- Harcourt teaching hospital (U.P.T.H) chemical pathology and Histopathology Laboratory.
Analysis of serum parameters:

Blood of each animal was centrifuged to obtain the serum which was used to assay for the serum activity of AST, ALT, and ALP. Also Creatinine, Bilirubin, Urea, Total protein and Albumin concentration was also estimated.

Histological examination:

Excised liver samples were fixed by immersion for the routine histological studies using formalin for 18 hours, dehydrated through series of graded alcohol, cleared in xylene, infiltrated and embedded in molten paraffin wax. Tissue blocks were sectioned at 6 μm thickness deparaffinized and stained with Haematoxylin and Eosin. The sections were examined with the light microscope and photomicrographs of the sections were taken for further analysis.

RESULTS

Physical and behavioural observation:

From observation made, there was no difference in behavioural changes noticed between the control group and experimental groups at the administered dosages. There was no mortality, stress or abnormal behavioural changes observed within the treated groups throughout the administration periods. Overt signs of toxicity such as lacrimation, squinting and, exophthalmia etc, were not expressed by the rats throughout period of study.

Biochemical assay:

The result of serum AST, ALT and ALP activity are shown in Table 2 below. For group 2, significant decreases at p ≤ 0.05 in the activity of some liver enzymes were observed after week 2 of administration. A significant increase at p ≤ 0.05 in these parameters was also observed in weeks 4 and 6. While for group 3, there was steady and significant increase in the activity of this enzyme when compared to the control group and also with group 2 at p ≤ 0.05.

The functionality of the liver was assayed by analysis of the total protein, albumin, creatinine and urea concentrations in serum. The values expressed as mean ± standard deviation are shown in Table 3.

Histological Observations

The histological observation of the livers showed distortion in cell architectures of the experimental groups. There were gross degeneration and necrosis observed in experimental groups and these observations were increased as the dosage of the medicinal formulation were increased (Fig 1 a–f and Table 4).

| TABLE 2: Effect of Yoruba medicinal formulation on serum AST, ALT and ALP activities |
|-------------------|-----------------|----------------|----------------|
| WEEK       | AST (IU/L)   | ALT (IU/L) | ALP (IU/L)    |
| 2  | 120.00 ± 1.63 | 30.00 ± 0.82 | 320.00 ± 0.82 |
| 4  | 120.00 ± 1.63 | 30.00 ± 0.82 | 320.00 ± 0.82 |
| 6  | 120.00 ± 1.63 | 30.00 ± 0.82 | 320.00 ± 0.82 |

Values are expressed as Mean ± Standard deviation of triplicate determinants at p ≤ 0.05.
### TABLE 3: Effect of Yoruba medicinal formulation on serum total protein, albumin, creatinine and urea concentrations

<table>
<thead>
<tr>
<th>GROUP</th>
<th>WEEK</th>
<th>GROUP 1 (CONTROL)</th>
<th>GROUP 2 2.9µl/Kg body weight</th>
<th>GROUP 3 5.5µl/Kg body weight</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Total Protein (g/l)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>60.25 ± 0.50</td>
<td>56.00 ± 0.82</td>
<td>53.00 ± 0.82</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>60.25 ± 0.50</td>
<td>52.00 ± 0.82</td>
<td>45.75 ± 1.89</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>60.25 ± 0.50</td>
<td>55.25 ± 0.96</td>
<td>52.00 ± 0.82</td>
<td></td>
</tr>
<tr>
<td></td>
<td>46.50 ± 1.29</td>
<td>40.50 ± 0.58</td>
<td>35.15 ± 0.87</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>46.50 ± 1.29</td>
<td>35.00 ± 0.33</td>
<td>31.15 ± 1.35</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>46.50 ± 1.29</td>
<td>32.00 ± 0.82</td>
<td>27.20 ± 0.54</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ALB(g/L)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>46.50 ± 0.82</td>
<td>46.50 ± 1.29</td>
<td>46.50 ± 1.29</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>46.50 ± 0.82</td>
<td>40.50 ± 1.29</td>
<td>35.15 ± 0.87</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>46.50 ± 0.82</td>
<td>32.00 ± 0.82</td>
<td>27.20 ± 0.54</td>
<td></td>
</tr>
<tr>
<td></td>
<td>BIL(µmol/L)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>5.91 ± 0.11</td>
<td>7.13 ± 0.16</td>
<td>4.49 ± 0.04</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>5.91 ± 0.11</td>
<td>7.96 ± 0.31</td>
<td>6.39 ± 0.45</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>5.91 ± 0.11</td>
<td>8.17 ± 0.19</td>
<td>8.86 ± 0.06</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CRT(µmol/L)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>87.45 ± 0.76</td>
<td>85.78 ± 1.48</td>
<td>78.58 ± 0.31</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>87.45 ± 0.76</td>
<td>71.53 ± 1.04</td>
<td>61.99 ± 0.29</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>87.45 ± 0.76</td>
<td>68.74 ± 0.32</td>
<td>60.03 ± 0.05</td>
<td></td>
</tr>
<tr>
<td></td>
<td>UREA(mmol/L)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>5.80 ± 0.00</td>
<td>5.42 ± 0.02</td>
<td>4.87 ± 0.21</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>5.69 ± 0.01</td>
<td>4.92 ± 0.01</td>
<td>4.28 ± 0.02</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>5.78 ± 0.02</td>
<td>4.74 ± 0.03</td>
<td>4.09 ± 0.01</td>
<td></td>
</tr>
</tbody>
</table>

Values are expressed as Mean ± Standard deviation of triplicate determinants at p ≤ 0.05

### TABLE 4: Summary of observations of the histological examination.

<table>
<thead>
<tr>
<th>GROUPS</th>
<th>WEEK 2</th>
<th>WEEK 4</th>
<th>WEEK 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Section of liver shows hepatocytes arranged in rolls radiating from the portal triad. Also seen are a few dilated central hepatic veins</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Show foecal and variable degenerative changes in zone 3 hepatocytes. Marked vacuolar hepatocytic degeneration and inflammation. Congested vessels channels; periportal inflammation; apoptosis.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Also shows hepatic degeneration in zone 3. Hepatic necrosis and inflammation observed. Vascular congestion, apoptosis.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. Pictomicrograph of Liver of control and experimental groups at weeks 2, 4 and 6.
DISCUSSION

The Liver plays an important role in many metabolic processes as such; any disturbance in the Liver would affect the normal level of measurable biochemical parameters in this organ. Aspartate transaminase, alanine transaminase and alkaline phosphatase are marker enzymes present in high concentrations mainly in the liver. When liver cells are inflamed or damaged, these enzymes leak into the blood stream leading to a rise in the serum level of these enzymes (David, 1985; Nkosi et al., 2005). Alanine transaminase is selectively a liver parenchymal enzyme than aspartate transaminase and a sensitive indicator of acute liver damage (Shah et al., 2002). Thus elevation of these enzymes in our study may indicate inflammation or damage to the liver cells. These parameters served as a marker of alteration in hepatic architecture and structural integrity of experimental groups.

It was observed that at week 4, the level of liver enzymes (AST, ALT and ALP) has increased which is indicative of liver damage. This was further confirmed by results of liver histology; as a significant percentage of degeneration, inflammation and necrosis were observed at certain portions of the liver (Fig. 1b-1g). At week 6 there was a significant increase in the serum concentration of liver enzymes when compared to the treatment groups at weeks 2 and 4 and also with the control groups. This effect proved irreversible, as the level of these liver enzymes still increased despite termination of formulation administration.

Nerbert (1983) reported that damaged liver cells lose their ability to conjugate bilirubin or remove unconjugated bilirubin from the blood thus an increase in unconjugated bilirubin in the serum. The fact that the direct bilirubin was high in this study may thus indicate liver damage. The significant decrease at p ≤ 0.05 in the level of total protein, albumin, creatinine and bilirubin are an indication of the decreased functionality of the liver. Creatinine is actually a breakdown product of creatine, is made by the liver and transported to the muscles. Albumin is one of the several proteins made by the liver as such a decrease in its concentration would signal liver damage. Urea is produced by
the liver as a breakdown product of amino acids. So a reduction in its concentration would signal decreased hepatic functionality.

These results taken together with the alterations in the architecture of the liver may strongly indicate liver damage in the experimental groups compared with the control groups.

Histological studies revealed that despite the acclaimed positive effect of the formulation, there were gross negative effects as seen in Table 4.

**CONCLUSION:**

The Yoruba medicinal formulation used in this study at the doses and tenure of administration resulted in impaired liver functionality which was as a result of alterations in the architecture of the liver cells. The long term use of these Yoruba medicinal formulations is thus hepatotoxic at the dosage administered and as such great care should be considered in its usage.

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A REVIEW ON PHYTOCHEMICAL AND PHARMACOLOGICAL VALUES OF FRUIT PULP OF AEGLE MARMELOS

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ABSTRACT

In the traditional system of medicine, medicinal plants form the back-bone in India. The Phytochemical ingredients from these medicinal plants serve as key compounds in drug discovery and design. A diverse range of bio active molecules are produced by plants which make them a rich source of different types of medicines. Plants have unimaginable healing power. Aegle marmelos is commonly known as Bilva tree belong to family Rutaceae. This plant is considered as a medicinal tree as it has several curative properties in treating different diseases. The present study reports an overview about the medicinal plant, Aegle marmelos (Linn.) Correa (Bael). In particular, it provides information relating to the phytochemical, antioxidant, antidiabetic, antimicrobial, antidiarrheal activity and other therapeutic benefits.

KEY WORDS: Aegle marmelos, Medicinal plants, Phytochemical Screening, Antibacterial activity

Cite this article:
INTRODUCTION

India is considered as a bank of medicinal and aromatic plants. It is estimated that nearly 7500 of the 17000 higher plant (angiosperms) species have medicinal values (Prabhakar et al., 2013). The Ayurveda system of medicine uses about 700 species, Unani 700, Siddha 600, Amchi 600 and modern medicine around 30 species (Kushagra et al., 2011). These plants are used for health, fragrance, cosmetics etc. The fourth largest pharmaceutical industry is Indian pharmaceutical industry. The Cultivation of Medicinal and Aromatic plants is a good option in this semi-arid region. Medicinal plants provide rich source of novel drugs, modern medicines, food supplements, folk medicines, pharmaceutical intermediates, neutralceutical bioactive principles and lead compounds in synthetic drugs (Saradha and Annapoorani, 2012).

Phytochemical extracts from medicinal plants holds promises that can be used in all types of allopathic medicine due to their anti-viral, anti-tumoral and anti-microbial properties. India has occupied one of the twelve mega biodiversity centers having more than 45000 useful plant species. Nearly about 15 biotic provinces, 10 vegetative zone and 16 different agro climatic zones contribute to its unmatched diversity in the world (Prabodh et al., 2007).

Bael (Aegle marmelos (Linn.) Correa) belongs to family Rutaceae. Its golden colored fruit resembles golden apple hence the generic name-Aegle, and the species name is derived from marmelosin contained in the fruit. It is a divine tree having curative properties. Marmelosin derived from the pulp is laxative and diuretic (Bag et al., 2009). The bark contains tannin and the coumarin, aegelinol; also the furocoumarine, marmesin; umbelliferone, a hydroxyl coumarin; and the alkaloids, fagarine and skimmianine (Morton and Miami, 1987). Leaf contains alkaloid ‘Aegeline’ used as antiasthematic agent (Priya et al., 2013). The roots and fruits of A.marmelos possess antiamoebic and hypoglycemic activity (Ponnachan et al., 1993). Fruit of A.marmelos contains Aurapten, Marmelosin, Psoralen, Luvangetin, Marmelide, Tannin, Phenolic compound and has several curative properties in curing ailments like diarrhoea, gastric troubles, tonic, and constipation, digestive, stomachic and laxative. Root possesses Halopine, Alkaloid, Terpines, Coumarins and attributes for healing heart disorders, hypoglycemic, fever, antiamoebic and rheumatism (Pushpendra et al., 2012). In the Ayurvedic, Siddha and Unani systems of medicine in India, A. marmelos has occupied as an important herbal medicinal plant for the treatment of diabetes mellitus (Ganesh et al., 2011). In the Ayurveda system of medicine, Bael has been praised for its contribution in treating chronic diarrhea and dysentery (Chandra, 2006).

Many of the researchers have validated the pharmacological importance of different parts of Aegle marmelos which includes antioxidant, free radical scavenging antibacterial, antiviral, anti-diarrheal, hepatoprotective, anti-diabetic, cardioprotective, gastroprotective, anti- ulcerative colitis and radioprotective effects (Manjeshwar et al., 2011; Rajan et al., 2011; Anurag et al., 2014; Patel et al., 2012). As at present scenario, only a few articles are available on the phytochemical and pharmacological values of fruit pulp of A. marmelos, the present review attempts to summarize the different bioactive compounds present in the fruit pulp of the plant which contributes to its medicinal properties in curing different ailments.

TAXONOMY OF AEGLE MARMELOS

Bael (Aegle marmelos) is a tree, native to biodiversity rich India. It is considered as most sacred plant by the Hindus.

English names: Golden apple, Stone apple, Bengal quince.

Indian names: bil (Gujurat), bel (Assam), bil (Himachal Pradesh), bilpatra, kumbala, malura (Karnataka), kuvalum (Kerala), maredu
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Botanical Classification

Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Sapindales
Family: Rutaceae
Subfamily: Aurantioideae
Tribe: Clauseneae
Genus: Aegle
Species: marmelos

MORPHOLOGICAL DETAILS OF AEGLE MARMELOS

Habit- Tree

Description: Bael is a medium sized deciduous tree greater than 8 m tall. The tree has unusual branches with aromatic leaves, sweet scented and greenish-white flowers.

Leaves: The leaves are alternate, pale green, trifoliate, having a long petiole. The petiole is 3.2 cm long and the two lateral leaflets are almost sessile, 4.1 cm long, 2.2 cm wide along with terminal leaflet, 5.7 cm long, 2.8 cm broad, ovate to lanceolate, reticulate pinnate venation.

Flowers: The flowers are greenish white, sweetly scented and have Bisexual, actinomorphic, ebracteate, hypogynous, stalk. The stalk which holds the flower is 8 mm long. The calyx of the flower is gamosepalous and five-lobed. The corolla is polypetalous, with 5 petals, imbricate, leathery, pale yellow from above and green from beneath. The Androecium is consists of stamens of length 4 mm with polyandrous condition, numerous, basifixed, dehiscence longitudinally. The Gynoecium is light green with capitate stigma hosting terminal style. The Fruit of the plant is very smooth, woody in nature, 5–15 cm in diameter containing numerous seeds which are densely enclosed with fibrous hair and are entrenched in a thin aromatic pulp (Patel et al., 2012).

Origin and Distribution: Bael tree found its existence somewhere back in 800 B.C. The tree grows wild in dry forests on hills and plains of central and southern India, Northern Malaya, Java and Philippine Islands, Burma, Pakistan, Bangladesh, Sri Lanka. It is cultivated in some Egyptian gardens, Trinidad and in Surinam. It is also found in the hilly areas of Himalaya, Uttar Pradesh, Uttarakhal, Bihar, Chhatisgarh, Deccan Plateau and East Coast (Prabodh et al., 2007).

Nutritional values of Bael Fruit: Studies on Bael fruit shows that it consists of moisture 61.5 percent, minerals 1.7 percent, fibre 2.9 percent, fat 0.3 percent, protein 1.8 percent, and carbohydrates 31.8 percent per 100 grams of edible portion. The mineral and vitamin contents present in fruit includes calcium, carotene, phosphorus, iron, thiamin, riboflavin, niacin and vitamin C. Its calorific value is 137 (Panda, 2000; Morton and Miami, 1987).

Propagation: Bael fruit is commonly grown in nurseries and the young plantlet are transplanted into the field. Seedlings show great variation in form, size, quantity, texture of rind and quality of pulp and number of seeds. The flavor ranges from unlikable to pleasant. Therefore, superior types must be grown vegetatively (Morton and Miami, 1987).

Flowering/Fruiting: Flowers-May to June, Fruits-May–June of following year (Dinesh et al., 2011).

PHYTOCHEMICAL ANALYSIS AND THE METHODOLOGY FOR EXTRACTION

A. marmelos plant has been blessed with seven major phytochemicals such as alkaloids, cardiac glycosides, terpenoids, saponins, tannins, flavonoids and steroids which are biologically active and have been the major source in curing different diseases. In the past, many research has been done on this
The fruit pulp of Bael contains bioactive substances like carotenoids, tannins, flavonoids, terpenoids, alkaloids, pectins, reducing sugar, saponins, carboxyls, phlobatanins and steroids (Manjeshwar et al., 2011; Dhanaraj et al., 2011; Venkatesh et al., 2009). The detailed analysis and findings of phytocomponents in Fruit pulp of A. marmelos by different researchers has been described below.

### Alkaloids

Alkaloids have been considered as the largest class of secondary bioactive compounds present in plants which includes an array of compounds such as skimmianine, fagarine, aegelin, aegelinosides, anhydro marmelin which are found in Bael fruit (Manjeshwar et al., 2011). The qualitative study by Dhanaraj et al. (2011) showed the presence of alkaloids using Mayer's, Wagner's, Hager's, and dragoncliff's reagent and was found to be more in alcohol, water and chloroform extracts. Venkateshan et al. (2009) using dragoncliff's reagent has performed qualitative test to show the presence of alkaloids in different plant extracts of A. marmelos. Rajan et al. (2011) performed qualitative test both for aqueous and alcoholic plant extracts and found the presence of alkaloids only in alcoholic extracts of fruit pulp along with the presence of cardiac glycosides in aqueous extracts. Two alkaloids 4, 7, 8-trimetoxyfuroquinoline (skimmianine) and N-2-hydroxy-2-(4-methoxyphenyl)-ethylcinnamamide (aegeline) were isolated by Sugeng et al. (2001) from the plant parts (leaves, roots) of A. marmelos and was confirmed by spectroscopic analysis.

### Phenolic compounds

Phenolic compounds are aromatic secondary metabolites in plants which include a wide range of classification as soluble (phenol acids, flavonoids, quinines) and non soluble compounds (tannins, lignins, cell wall bound hydroxycinnamic acids) (Harborne, 2000). Phenols are aromatic compounds which offer resistance to diseases and pests in different plants. It includes an array of secondary metabolites like tannins and flavonoids. Rajan et al. 2011 using folin-ciocalteau reagent estimated quantitatively total phenolic contents in fruit pulp. The study showed the presence of tannins and phenolic compounds were more in aqueous extracts than alcoholic fruit extracts. In another study, Dhanaraj et al. (2011) showed the presence of tannins and phenols in alcohol and water extracts of both variant of A. marmelos. Venkateshan et al. (2009) showed the presence of tannins, phlobatanin, and terpenoids in ethanolic extracts of A. marmelos qualitatively. Total phenolic and flavonoid contents of different parts extract of A. marmelos was carried out by Nadeem et al. (2010) using Folin Ciocalteu reagent and found leaf contains larger amount of these phytocomponents than other parts of the plant.

### Flavonoids

Flavonoids are bio active compounds which normally accumulate in plant body as secondary metabolites in large quantities. Anthocyanin and Leucocyanin are the flavonoids present in Bael fruit (Manjeshwar et al., 2011). Venkateshan et al. (2009) noticed the presence of flavonoids in ethanolic extracts of A. marmelos which relates its role as an antimicrobial activity against tested bacteria such as E. coli, Pseudomonas aeruginosa and Bacillus subtilis. Quantitatively, Rajan et al. (2011) estimated total flavonoids content using aluminium chloride colorimetric method and the study showed the presence of flavonoids was more in alchololic extracts (166.33 ± 09.60 mg/g) than the aqueous extracts (129.00 ± 07.00 mg/g) in fruit pulp of A. marmelos (*p<0.05).

### Other chemical constituents of Bael fruit

Literature shows the presence of wide variety of chemicals in fruit pulp of Bael which contributed to its anti-microbial and medicinal properties. Pulp contains coumarins like marmelosin, aegeline, marmelein, alloimneeratorin, psoralen, marmelide (Uttara
et al., 2012). Fruits of Bael also contain tartaric acid, pectins, linoleic acid and terpenoids (Manjeshwar et al., 2011). Seed contains different oil compounds (terpenoids) such as essential oil –D- limonene, Cineol, Citral, P-cymene, Cumin aldehyde, A-D-phellandrene and Citronellal (Pushpendra et al., 2012). Polysaccarides like galactose, uronic acid, arabinose are isolated from fruit pulp on hydrolysis (Prabodh et al., 2007). Tannins such as skimmianine (4,7,8-trimetoxyfuro,quinoline) and Carotenoids which are helpful in imparting colours to the fruit such as umbelliferone are also noticed in fruit pulp of A. marmelos (Patel et al., 2012).

ANTI MICROBIAL AND PHARMACOLOGICAL PROPERTIES OF BAEL FRUIT

Bael tree is a gift from God to mankind as it has several medicinal properties in curing various ailments and diseases affecting people in both developing and developed countries. Several studies have been done to validities the anti microbial and pharmacological properties of Bael fruit.

Antioxidant activity

Antioxidants are the natural occurring compounds produced during oxidative stress with strong free radicals scavenging activity helpful in protecting the plants. Many antioxidant compounds such as flavonoids, flavones, isoflavones, coumarin, anthocyanin, lignans, catechins and isocatechins are found in the fruit pulp of A. marmelos (Maity and Hansda, 2009). Free radical scavenging activity and antioxidant activity of both ripe and unripe fruits were conducted by Sharmila & Vasundra, (2011) to compare in-vitro antioxidant activity of the ethanolic extract of ripe and unripe fruit of A. marmelos and the study indicated that the enzymatic antioxidants increased in ripe fruit when compared to unripe fruit extract (except glutathione peroxidase). Rajan et al. (2011) studied the antioxidant potential of both aqueous and alcoholic extracts of fruit pulp using DPPH standard assay. The extracts showed significant free radical scavenging action against nitric oxide. Several antioxidative parameters like glutathione reductase reduced glutathione, super oxide dismutase (SOD), glutathione peroxidase and catalase have shown an increase in their dose–related activity and decrease in lipid peroxidation when treated with Bael leaf extract (Sabu and Kuttan, 2004). DPPH radical scavenging assay showed the efficient antioxidant activity of fruit pulp in the aqueous extracts compare to other extracts (Gheisari et al., 2011). Hence from the above it can be stated that different extracts of Beal shows antioxidant activity in protecting the plant in various oxidative stress conditions which has to be further analyze in order to make a hypothesis which can be implemented in curing prevailing disorders.

Antidiabetic activity

Diabetes is a common major metabolic disease prevailing in the present scenario and most of the populations are suffering with it, where cure becomes inevitable. Hence plant products and different animal models have been exploited to find the solution in overcoming this disease. In this regards, Bael plant has become an icon and helps in stimulating glucose uptake mechanism similar to insulin treatment (Upadhya et al., 2004). Lowering of Hypoglycemic effect was shown using aqueous extracts of Fruit of Bael against STZ induced diabetes rats and in rabbit model, alcoholic extracts shown its effect in lowering the glucose level when oral administration was done (Patel et al., 2012). The study by Sevugan et al. (2008) shown that the leaf and callus extracts possess the ability to stimulate the insulin secreting cells of pancreas. Among the various extracts used, the methanol extracts of the leaf and callus revealed the maximum anti-diabetic effect. The results suggested that both the callus and leaf materials contain anti-diabetic active principles, which reduced the sugar level in STZ-diabetic rabbits. Aqueous extract of A. marmelos fruits can be used as an anti-hyperlipidaemic agent as found in the streptozotocin-induced diabetic wistar rats.
(Marzine and Gilbart, 2005). As it is believed that India is going to be the capital city in the world in the terms of number of populations suffering with diabetics, it becomes utmost importance in science and technology field to explore these hidden medicinal properties of plant such as A. marmelos in solving the issues related to diabetics in near future.

**Antimicrobial activity of fruit pulp**

Different parts of A. marmelos plant have been found to inhibit the growth of various pathogenic micro-organisms. Several micro-organisms including fungi and bacteria have shown its growth inhibition effect in spreading a diseases when treated with different extracts of Bael. Rajan et al. (2009) studied different extracts of fruit pulp of A. marmelos against Escherichia coli, Shigella, Salmonella sp and hypothesized that the phytochemicals including Flavones, Coumarin and Tannins were effective against all. The crude ethanolic extracts of Bael fruits were effective against the tested organisms Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa and Bacillus subtilis due to the presence of chemicals like Alkaloids, Cardiac glycosides, Terpenoids, Saponins, Tannins, Flavonoids, and Steroids (Venkateshan et al., 2009). Using methanol and ethanol extracts, Ankur et al. (2010) evaluated the immunomodulatory activity in rats and found that the methanolic extract possess higher potential degree in stimulating cell mediated and antibody mediated immune response as compared to ethanolic plant extracts. Vijay et al. (2010) attributed the presence of coumarins, alkaloids, sterols and essential oils in possessing the properties like anti-microfilarial, hypoglycaemic, antidislipidemic, immunomodulatory, antiproliferative, and wound healing, anti-fertility, antifungal, analgesic, anti-inflammatory, antipyretic and insecticidal activity in different parts of A. marmelos. The antifungal activity of the leaves was tested against clinical isolates of dermatophytes such as Trichophyton mentagrophytes, T. rubrum, Microsporum canis, M. gypseum, Epidermophyton floccosum (Balakumar et al., 2011). Hence from these studies we can conclude that an elaborate investigation has to be made in order to correlate the importance of these bioactive constituents in antimicrobial properties shown in different plant extracts.

**Antidiarrheal Activity**

Gastrointestinal infections (Diarrhoea and Dysentery) are now days the major cause of morbidity and mortality in the developing countries. Since from the ages man has born, exploring and exploitation of the plants has been a routine work in treating this global problem. In this regard, the unripe and half ripe fruit of Bael has been extensively used as the remedy (Prabodh et al., 2007). Crude aqueous extract of unripe fruits exhibited inhibitory activity against Giardia and rotavirus, the causative organisms for diarrhoea (Brijesh et al., 2002). The unripe fruit of Bael can be used in different combinations in cure of chronic diarrhea and the fruit pulp possess antiprotozoal activity which can be explored in treatment of dysentery and loose motions (Gupta et al., 2011).

**Miscellaneous Uses**

Bael is a medicinal plant and possesses a wide variety of medicinal properties. Apart from the uses mentioned above its contribution has been marked significantly in the area of insecticidal activity (Kumar et al., 2008; Dinesh et al., 2011), Antispermatogenic Activity (Sur et al., 1999), anti-lipid-peroxidative activity, Toxicity Studies (Veerappan et al., 2007), Anti thyroid Activity (Dinesh et al., 2011; Panda and Kar, 2006), Anticancer Activity (Leticia and Costa, 2005; Gagetia et al., 2005), Hepatoprotective activity (Singanan et al., 2007; Rammik and Harwinder, 2008). This plant can be cultivated on waste land and unproductive agricultural areas and can be use as a medicinal plant on daily basis due to its blessed medicinal values in curing different ailments, diseases and disorders.
CONCLUSION

It is quite evident from this review that _Aegle marmelos_ is a divine tree which has taken an important place in _Ayurveda, Unani, Siddha_ traditional system of medicine. The plant has various therapeutic applications due to its blessed presence of phytoconstituents. Almost all parts of the plant have been used for the treatment of various diseases. Thus, upon conclusion, this review demonstrates the applications of the bioactive compounds of _A. marmelos_ in a single roof, thereby paving way for the plant researchers to explore this plant for wider applications in the near future that might enable mankind to get maximum benefit from the Nature and Natural products.

REFERENCES


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BOTANICALS FOR MANAGING CARDIOVASCULAR DISORDERS: A REVIEW OF MEDICINAL WEEDS ON KNUST CAMPUS

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ABSTRACT

Cardiovascular diseases (CVD) are the major cause of mortality and morbidity throughout the world, claiming more than 17.1 million lives each year. These diseases are caused by dyslipidemia, lack of physical activities, smoking, high levels of low-density lipoprotein (LDL) cholesterol, oxidative stress and excessive alcohol consumption. Natural products have played a significant role in drug discovery and development especially for agents against cancer and infectious disease. Natural compounds possess highly diverse and complex molecular structures and often provide highly specific biological activities. Ethnopharmacological use of plant-derived natural products has been a major source for discovery of potential medicinal agents. A wide variety of extracts from these plants have been used for about a century as alternative source of medical care for most of the population of the developing world. The extracts of some medicinal plants treat cardiovascular diseases without affecting coronary blood flow. Phytochemicals such as carotenoids, flavonoids, cinnamic acids, phenolics and proanthocyanidins possess antioxidant properties which enable them to play a significant role in the adsorption and neutralization of free radicals mainly due to their redox properties. This review focuses on the medicinal weeds grown on the main campus of the Kwame Nkrumah University of Science and Technology, Kumasi-Ghana with documented evidence of use in the management of cardiovascular disease.

KEYWORDS: Cardiovascular diseases, Medicinal plants, Phytochemicals, Antioxidants, flavonoids.

Cite this article:

INTRODUCTION

The World Health Organization (2007) reported that cardiovascular diseases (CVD) are the major cause of mortality and morbidity throughout the world. The World Heart Federation (WHF, 2011) estimated that 17.1 million lives are claimed by the cardiovascular diseases each year and stated that these diseases are among the most widespread and costly health problems facing many nations today. According to the Centre for Disease Control (CDC, 2009), about one third of all deaths recorded in the United States were caused by CVDs. A 5-year retrospective study in a major teaching hospital in Ghana has indicated that about 22.5% of all deaths within the period were cardiovascular in nature (Sanuade et al., 2013). Walden and Tomlinson (2011), suggested the major causes of these diseases to be insufficient consumption of fruits and vegetables, dyslipidemia, lack of physical activities, smoking, high levels of low-density lipoprotein (LDL) cholesterol, oxidative stress and excessive alcohol consumption. Drug treatment of conventional risk factors has been very effective in reducing cardiovascular events such as lowering LDL and treatment of hypertension (Anderson et al., 2007; Turnbull et al., 2008).

Recent studies have revealed that there is growing awareness of the use of medicinal plants in the prevention and treatment of CVD (Walden and Tomlinson, 2011). Kumar et al. (2011) reported that about 80% of the world’s population rely on traditional medicines for their primary health care which is predominantly based on plant materials. They have been effectively used worldwide to control heart diseases and other conditions (Walden and Tomlinson, 2011; Mwitari et al., 2013; Ghulam et al., 2013). A wide variety of extracts from these plants have been used for about a century as alternative source of medical care for most of the population of the developing world (Ghulam et al., 2013). Walden and Tomlinson, (2011) reported that the extracts of some medicinal plants have cardioprotective effects and treats cardiovascular diseases without affecting coronary blood flow. According to Lokhande et al. (2005), in Ayurvedic preparations, medicinal plants are used extensively for the treatment of many cardiac disorders such as angina, hypertension, myocardial infarction, cardiomypathes, congenital heart diseases and other cardiovascular diseases.

Doughari et al. (2009) reported that the medicinal values of these plant extracts are due to the presence of phytochemicals. These include antioxidant compounds that play a major role in the adsorption and neutralization of free radicals mainly due to their redox properties. The antioxidant compounds act as reducing agents and singlet oxygen quenchers (Walden and Tomlinson, 2011). Plant based antioxidant compounds include carotenoids, flavonoids, cinnamic acids, phenolics and proanthocyanidins used for cardiovascular disease (Olayinka and Okoh, 2009).

Recent investigations have been undertaken that suggest a correlation between phytochemicals intake and reduced risk of cardiovascular disease (Ullah and Khan, 2008). Epidemiological studies suggest that flavonoids are effective in the prevention of diseases associated with oxidative damage of biomolecules, thus can help lower the risk of coronary heart diseases (Olayinka and Okoh, 2009). Flavonoids’ ability to scavenge oxidants enable them to lower peroxidative tendencies and retard coronary artery disease, myocardial infarction, atherogenesis and thrombosis (Ullah and Khan, 2008). Proanthocyanidins are antioxidants that inhibit lipid peroxidation and have anti-inflammatory and antiallergenic properties (Walden and Tomlinson, 2011). Thus the identification of medicinal weeds, which hitherto are controlled and/or destroyed by both chemical and physical means, and characterization of phytochemicals present in them will provide evidential usage for managing human ailments including CVDs. This review paper mainly focuses on the medicinal weeds identified on the main campus of the Kwame Nkrumah University of Science and Technology (KNUST), Kumasi-Ghana that
could be used to manage and control cardiac disorders. The KNUST is the main public science and technology university in Ghana and the environment serves as habitat for both flora and fauna. Biomedical scientists in the university are engaged in pharmacological evaluation including cardiotonic effects of extracts from these plants and animals. The summary of some identified plants are as shown in Table 1. All plants were certified by Dr. George H. Sam of the Department of Herbal Medicine (KNUST, Kumasi) and a specimen was deposited at the department’s herbarium.

Table 1. Summary of medicinal weed used for managing cardiac disorders

<table>
<thead>
<tr>
<th>Scientific Name</th>
<th>Family Name</th>
<th>Part Used</th>
<th>Cardiotonic Agents</th>
<th>Studies Carried</th>
<th>References</th>
<th>Voucher Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acanthospermum hispidum DC</td>
<td>Asteraceae</td>
<td>Whole plant</td>
<td>Flavonoids</td>
<td>Ethnomedical studies</td>
<td>(Evani et al., 2008)</td>
<td>KNUST/HM1/2014/L050</td>
</tr>
<tr>
<td>Boehravia repens L.</td>
<td>Nyctaginaceae</td>
<td>Root</td>
<td>Flavonoids and terpenes</td>
<td>Ethnomedical studies</td>
<td>(Santhosha et al., 2012)</td>
<td>KNUST/HM1/2014/L051</td>
</tr>
<tr>
<td>Celosia trigyna L.</td>
<td>Amaranthaceae</td>
<td>Whole plant</td>
<td>Flavones</td>
<td>Ethnomedical studies</td>
<td>(Denton, 2004)</td>
<td>KNUST/HM1/2014/L052</td>
</tr>
<tr>
<td>Cleome viscosa Linn.</td>
<td>Capparaceae</td>
<td>Whole plant</td>
<td>Flavonoids</td>
<td>Ethnomedical studies</td>
<td>(Ahmed et al., 2011)</td>
<td>KNUST/HM1/2014/L053</td>
</tr>
<tr>
<td>Dissotis rotundifolia (Sm) Triana</td>
<td>Melastomataceae</td>
<td>Leaves</td>
<td>Cardiac glycosides</td>
<td>Ethnomedical studies</td>
<td>(Abere et al., 2010)</td>
<td>KNUST/HM1/2014/L054</td>
</tr>
<tr>
<td>Gongrenema latifolium Benth</td>
<td>Apocynaceae</td>
<td>Stem bark</td>
<td>Polyphenolics</td>
<td>Methanol and aqueous studies</td>
<td>(Oguwike et al., 2013)</td>
<td>KNUST/HM1/2014/L055</td>
</tr>
<tr>
<td>Launaea taraxifolia (wild) Amin ex C. Jeffrey</td>
<td>Asteraceae</td>
<td>Leaves</td>
<td>Flavonoids</td>
<td>Ethnomedical studies</td>
<td>(Dickson et al., 2012; Adinortey et al., 2012)</td>
<td>KNUST/HM1/2014/L056</td>
</tr>
</tbody>
</table>

**ACANTHOSPERMUM HISPIDUM DC**

**Description:** *A. hispidum* DC is an erect annual herb that belongs to the family Asteraceae, originated from tropical America and commonly known as the Britsly starbur, Goat’s head, Hispidstarburr and Starbur (Anup et al., 2012). The plant has a characteristic light, slightly sweet aroma and found in a wide range of habitats. It is commonly found in cultivated upland crops, roadsides, pastures, waste areas, around corrals, and along railroads and cattle trails and is particularly adapted to light textured soils but also grows well in heavy textured soils (Evani et al., 2008; Anup et al., 2012). It also grows in cultivated areas of KNUST.

**Parts used:** Whole plant (Anup et al., 2012)

**Investigational uses:** Evani et al. (2008) reported that the plant has been used traditionally for the treatment of hypertension.

**Phytochemical studies:** Harekrisha et al. (2010) reported that the petroleum ether extracts of *A. hispidum* contained only terpenoids but chloroform and ethanol extracts exhibited the presence of carbohydrates, alkaloids, glycosides, flavonoids, tannins and saponins. According to Evani et al. (2008), the leaves of *A. hispidum* contain caffeic acid and phenylpropanes, sesquiterpene hydrocarbons, β-caryophyllene, α-humulene, bicyclogermacrene, germacrene D, α-bisabolol, nonanal, carvacrol and methyl carvacrol.

**Most active phytochemicals:** Flavonoids

The presence of flavonoids in the plant makes it beneficial in managing hypertension. Schaeffer (2012) stated that several studies have demonstrated that flavonoids can significantly lower systolic blood pressure. Plants high in flavonoids appear to lower systolic blood pressure remarkably as well as LDL cholesterol-lowering and HDL-raising.
without the risk of weight gain. Epidemiologic studies also suggest that higher polyphenol intake from plants are associated with decreased risk for cardiovascular disease (Schaeffer, 2012; Walden and Tomlinson, 2011). In addition, phytochemicals have been shown to have roles in the reduction of platelet aggregation, modulation of cholesterol synthesis and absorption, and reduction of blood pressure (Walden and Tomlinson, 2011).

Other medicinal uses: *A. hispidum* has reportedly been used traditionally in the form of a paste to treat skin ailments, jaundice, malaria, vomiting, cephalgias, headache, abdominal pain, convulsions, stomachache, constipation, eruptive fever, snake bite, epilepsy, blennorrhoea, hepato-biliary disorders, malaria, microbial infection and viral infections (Anup et al., 2012; Tijani et al., 2013).

Pharmacological activities: The plant has been suggested to possess abortifacient and teratogenic, antiviral, antiobdiarrheal, antitumour, anthelmintic, antimicrobial, antiplasmodial, antifeedant, antipyretic, sudorific, depurative, astringent, abortive, and diuretic activities (Evani et al., 2008; Anup et al., 2012).

Toxicology: Both seeds and leaves contain phenolic acids that are allelopathic to other plants (Anup et al., 2012). Studies in mice showed that ingested seeds were toxic and resulted in liver damage, glomerular atrophy, congestion and hemorrhaging in the spleen, the lungs and the heart and catarhal enteritis (Evani et al., 2008).

**BOERHAVIA REPENS L.**

Description: *Boerhavia repens* is a terrestrial annual to perennial herb that belongs to the family Nyctaginaceae (Avijit et al., 2013). It is commonly called spreading hogweed, creeping spiderling, red hogweed in English and has a pantropical distribution. It is distributed throughout regions with a distinct dry season in Africa. It can also be found in India (Avijit et al., 2013). *B. repens* occurs in disturbed sandy and rocky localities, often in occasionally inundated areas, such as ditches along roadsides, dry river beds, flood plains and irrigated fields.

**Parts used:** Root, leaves and seeds (Mahesh et al., 2012).

**Investigational uses:** Used as cardiotonic (Santhosha et al., 2011).

**Phytochemical studies:** Phytochemical screening of *B. repens* revealed the presence of liriodendrin, punarnavoside, boerhavine and potassium nitrate, rotenoid, flavonoid glycosides, the alkaloid punarnavine, flavonoids, steroids, triterpenoids, lipids, lignins, carbohydrates, hypoxanthine 9-larabinofuranoside, ursolic acid, punarnavoside, liriodendrin and glycopeptides (Santhosha et al., 2011; Mahesh et al., 2012).

**Most active phytochemicals:** Flavonoids and terpenes.

For a drug or chemical to be called a cardiotonic, it should contain cardiotonic agents that strengthen the heart output and serve as a stimulant to the heart. According to Olayinka and Okoh (2009), many studies have revealed that flavonoids have antioxidant properties and hence prevent low density lipoprotein oxidation *in vitro* and so may play a role in the prevention of coronary heart disease (CHD). The intake of flavonoids has been found to be inversely correlated with the plasma total cholesterol and low-density lipoprotein (LDL) cholesterol concentrations thereby revealing the potential of flavonoids in the reduction of risk for coronary artery disease (Walden and Tomlinson, 2011). Triterpenes are very important phytochemicals which have the potential to treatment of cardiovascular diseases. The triterpene glycosides are believed to be the primary active components used for recovery from heart attacks. The triterpenes lower blood lipids and enhance oxygen utilization and may have cardiac protective effects (Siddique and Sallem, 2011).
**Other medicinal uses:** The plant has been reported by Mahesh *et al.* (2012), to have numerous medicinal uses. It aids in the treatment of liver disorders such as jaundice, hepatitis, cirrhosis, anaemia, detoxification and treats chemical injury, kidney urinary tract disorders and obesity (Mitra and Mukherjee, 2010).

**Pharmacological activities:** It has been demonstrated that the plant exhibits various pharmacological and biological activities such as aphrodisiac, antimalarial, hepatoprotective, anti-convulsant, anthelmintic, anti-inflammatory, anti-flatulent, appetite stimulant, abortifacient, anti-fibrinolytic, anti-metastatic and aphrodisiac activities (Santhosha *et al*., 2011). The chloroform and methanol extracts of the roots and aerial parts of *B. repens* exhibited hepatoprotective activity against carbon tetrachloride intoxication in experimental rats. Hepatoprotective activity of 50% aqueous alcohol extract of the whole plant against experimentally induced carbon tetrachloride hepatotoxicity in rats and mice was also observed (Santhosha *et al*., 2011).

**CLEOME VISCOSA LINN.**

**Description:** *Cleome viscosa* Linn., commonly known as thick weed or spider plant belongs to the family Capparaceae. It is an annual sticky herb found in India and throughout the tropics of the world. According to Saradha and Subba (2010), it occurs mostly in woodland and grassland, and is a weed of fallow land, fields, roadsides and wasteland, often occurring on sandy soils.

**Investigational use:** Cardiac stimulant and management of cardiac disorders (Ahmed *et al*., 2011).

**Phytochemical studies:** Koche *et al.* (2010) and Jane and Patil (2012) reported the presence of alkaloids, tanninoids, sapogenins and terpenoids in the leaves of *Cleome viscosa*.

**Most active phytochemicals:** Flavonoids

**Other medicinal uses:** The leaves and seeds are used as a rubefacient and vesicant and to treat infections, rheumatism, diarrhoea, fever, inflammation and mental disorders (Jane and Patil, 2012).

**Pharmacological activities:** The seeds and oils of the weed have anthelmintic properties but they are ineffective in treating roundworm infections, analgesic activity in mice and local anaesthetic activity in guinea pigs. In tests with rats, the anti-diarrheal and antipyretic activities of the extracts have been confirmed. It has also been reported to possess hepatoprotective, immunomodulatory, carminative, antisepic, sudorific, irritant, acrid, rubefacient and vesicant activities (Mali, 2010; Ahmed *et al*., 2011).

**CELOSIA TRIGYNA L.**

**Description:** *Celosia trigyna* L. is an annual erect herb which belongs to the family Amaranthaceae. It is commonly called silver spinach, wool flower, and cock’s comb in English. *C. trigyna* occurs almost throughout tropical Africa, South Africa and southern Arabia and is regarded as a weed but is used as a leafy vegetable in Benin and southern Nigeria. It is found in forest clearings and grassland, along roadsides and rivers, and as a weed in fields. It grows on a wide range of soils, but prefers fertile well-drained loamy soils (Denton, 2004).

**Parts used:** Whole plant, leaves and flowers (Denton, 2004).

**Investigational uses:** Treatment of heart complaints (Denton, 2004).

**Phytochemical studies:** Flavones, glycosides, saponins, steroids, tannins and alkaloids.

**Most active phytochemicals:** Flavonoids

Potential biological mechanisms including: anti-oxidant, anti-inflammatory, reduced LDL cholesterol oxidation, regulated endothelial nitric oxide synthesis and inhibition of platelet function (Denton, 2004).
**Other medicinal uses:** It is used traditionally for the treatment of kidney disorders, liver diseases, menstrual cycle problems, pulmonary troubles, stomach troubles and venereal diseases. In Ghana it is applied to sores and boils to heal (Denton, 2004).

**Pharmacological activities:** Pharmacological investigation of the plant showed that the plant serves as vermifuge and diuretic and has anthelmintic properties (Denton, 2004).

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**DISSOTIS ROTUNDIFOLIA (SM) TRIANA**

**Description:** *Dissotis rotundifolia* Triana, is a perennial herb commonly called Pinklady. It belongs to the family Melastomataceae and is a native of tropical West Africa (Mann et al., 2009).

**Parts used:** Whole plant and leaves (Abere et al., 2010)

**Investigational uses:** Managing circulatory problems (Abere et al., 2010).

**Phytochemical studies:** Phytochemical evaluation revealed the presence of alkaloids, cardiac glycosides, saponins and tannins (Mann et al., 2009).

**Most active phytochemicals:** Cardiac glycosides

The cardiotonic agents are agents that have a strengthening effect on the heart or that can increase cardiac output. These agents include cardiac glycosides and are used after myocardial infarction, cardiac surgical procedures, in shock and in congestive heart failure. The presence of cardiac glycosides therefore makes *D. rotundifolia* very vital medicinal source for the treatment of heart problems. Cardenolides, for example, inhibit the Na⁺/K⁺ -ATPase pump in mammals. Several plants with cardiac glycosides or cardenolides are used medicinally and often used to treat heart problems (Piacente et al., 2009).

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**Other medicinal uses:** In Nigeria, *D. rotundifolia* is used mainly for the treatment of rheumatism and painful swellings. The leaf decoction is used to relieve stomach ache, diarrhoea, dysentery, cough, stop abortion, conjunctivitis, circulatory problems and venereal diseases (Abere et al., 2010). In East Africa the plant is used for the treatment of bilharzias (Abere et al., 2007).

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**GONGRONEMA LATIFOLIUM BENTH**

**Description:** *Gongronema latifolium* is a shrub that belongs to the family Apocynaceae. It is widespread in tropical Africa.

**Parts used:** Whole plant and Stem bark

**Investigational uses:** Antihypertensive (Oguwike et al., 2013).

**Phytochemical studies:** The plant contains phytochemicals such as polyphenols, alkaloids, glycosides, flavonoids, terpenes, tannins, saponins, alkaloids, β-sitosterol, lupenyl esters, pregnane ester and essential oils (Nnodim et al., 2012).

**Most active phytochemicals:** Polyphenolic acids and flavonoids

Quiñones et al. (2013) reported in their study that in recent years, numerous studies have demonstrated the health benefits of polyphenols against cardiovascular diseases. These polyphenols present vasodilator effects and are able to improve lipid profiles, attenuate the oxidation of low density lipoproteins and can modulate apoptotic processes in the vascular endothelium due to their antioxidant properties.

**Other medicinal uses:** It is used to treat malaria, stomach disorders, diabetes, muscular pains, arthritis and inflammation, cough and loss of appetite. It has also been reported that the plant is used for the treatment of sore gums, colic, dyspepsia, worm infections and for maintaining healthy blood glucose level (Akuodro et al., 2010).
Pharmacological activities: *G. latifolium* is reported to have anthelmintic, anti-inflammatory, antibacterial, antioxidant, anti-asthmatic and antiplasmodial activities. The leaf extracts have analgesic effects, antipyretic, antisickling activities. The stem bark extracts have anti-ulcerative property (Oguwike et al., 2013).

LAUNAEA TARAXIFOLIA (WILLD.) AMIN EX C. JEFFREY

Description: *Launaea taraxifolia* is a perennial herb usually called dandelion. It belongs to the family Asteraceae and occurs mostly in the Tropical West Africa, Mexico, West Indies, Central and South America, Europe, North Africa, Atlantic Islands, South, West and Central Asia. It grows in an open habitat and is considered as weed.

Part used: Whole plant and leaves

Investigational uses: Heartburns and lower blood pressure (Adinortey et al., 2012).

Phytochemical studies: Phytochemical screening by Dickson et al. (2012), revealed the presence of alkaloids, glycosides, terpenes, flavonoids and phytosterols. The leaves also contain cardiac glycosides, terpenoids, tannins, saponins and steroids (Adinortey et al., 2012).

Most active phytochemicals: Flavonoids and terpenes.

Some of these metabolites act as natural antioxidants to neutralize the harmful effect of oxygen radicals in the body. One of the major classes of natural antioxidants found in plants that remove such free radicals is polyphenols.

REFERENCES


The phenolic compounds (flavonoids and tannins) are able to neutralize reactive oxygen and nitrogen species and also break down peroxides. The presence of these phenolic metabolites in the *L. taraxifolia* are notably helpful as their utilization would protect the individual from some of the free radical mediated diseases such as Alzheimer's, cardiovascular diseases and cancer (Cartea et al., 2011).

Other medicinal uses: The plant has been traditionally used as remedy for abdominal disorders, liver diseases, skin, conjunctivitis, measles and diabetes (Gbadamosi et al., 2012; Adinortey et al., 2012).

Pharmacological activities: From indigenous knowledge, Dansi et al. (2012) noted that through simple and regular consumption as leafy vegetable, the plant has lactogenic, antibiotic, antimalarial, antioxidant, anti-hyperglycemic, anti-inflammatory, hypercholesterolemic, anti-cancer, antimicrobial and antidiabetic activity. The leaf extract of the plant has been observed to have antiviral potentials and has cholesterol lowering effect (Obi, 2011; Dickson et al., 2012).

CONCLUSION

To avert cardiovascular diseases as the world's leading killer among non-infectious diseases, it becomes more important to identify plants materials that are very relevant to the managements of cardiac metabolic disorders and further investigated to extract some important secondary metabolites that can serve as the source of therapeutic agents for managing cardiac disorders.


GUGGULU [COMMIPHORA WIGHTII (Arn.) Bhandari] AND ITS FORMULATIONS IN BRIHATRAYEE - A REVIEW

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ABSTRACT

Guggulu [(Commiphora wightii (Arn.) Bhandari]. and its formulations are frequently used since vedic period. A meticulous screening was done through Brihatrayee to analyse all formulations that contain Guggulu in their composition. Maximum formulations that hold Guggulu as a component were found to be liquids or semi-liquids or semi-solids. But, in current scenario, most of the Guggulu based formulations are available in solid forms like pills or tablets. As Guggulu pills are associated with problems related to disintegration, physicians advocate crushing them before their internal administration. Possibly, observing this inconvenience; seers of brihatrayee preferred dispensing Guggulu in liquid media that will by-pass the problem of disintegration and the associated inconveniences. This review makes clear that, solid form of Guggulu Kalpa (like pills or tablets) is a latest pharmaceutical development that probably took place to have certain added advantages.

KEY WORDS: Ashtanga hridaya, Charaka samhita, Commiphora wightii, Guggulu, Sushruta samhita

Cite this article:

INTRODUCTION

To overcome inconveniences of dosage forms like powders etc., seers preferred solid dosage forms, where the active medicament will be presented in a compact form. One of such inventions is conversion of the raw material into Vati (pills). In this kind of dosage form, the medicament or the active therapeutic agents will not come in contact with external factors. Hence, the product will remain potent comparatively for a longer duration than that of certain other dosage forms like powder or decoction. On due course of time, they (vati) became an important, widely used dosage forms and occupied a significant seat in Ayurveda therapeutics and modern as well (R.M. Mehta, 2010). As they provide a number of advantages to the patient, prescriber, manufacturer and the pharmacist, their popularity is further increasing gradually.

Vati are made-up of fine powders of raw drugs of plant, mineral or animal origin that are levigated with certain liquid medias like swarasa (juice) or kwatha (decoction) or water or honey or any other specified liquid media till attaining pill rolling consistency (Vidhyasagar P, 2005). The mass will be rolled into pills of desired size and shape manually and stored for further therapeutic applications. When pills are made by Guggulu, they are familiarly known as Guggulu Vati. Various Guggulu vati are mentioned in Ayurvedic textbooks. Considering the wider publicity, therapeutic utility; Ayurvedic Formulary of India discussed Guggulu kalpa in a separate chapter (Anonymous, 2003).

In due course of time Guggulu Vati became commonly observed part of a prescription due to their effectiveness, and additional advantages like ease in dose fixation etc. As Guggulu Vati is comparatively harder; they may take more time for disintegration. Considering this, physicians generally advice crushing them before swallowing for better absorption.

It was observed on a casual reading through Brihatrayee that seers often preferred to dispense Guggulu in liquid or semi-liquid forms. This may be to bypass the longer disintegration time. Considering this, a meticulous screening was done through Brihatrayee to analyse all formulations that contain Guggulu in their composition.

MATERIALS:

A review has been made through Charaka samhita (Acharya YT, 2005), Sushruta samhita (Acharya YT, 2003), Ashtanga Sangrahra (Atrideva Gupt, 2005) and Ashtanga Hridaya (Pandit B.H. Paradkar, 2005). Commentaries of Chakrapani (on Charaka samhita), Dalhana (on Sushruta samhita), and Indu (Sharma S., 2012) (on Ashtanga sangrahra) were also screened during the attempt.

OBSERVATIONS & RESULTS:

Characteristics and Types

Guggulu possesses Katu Rasa (pungent taste), Laghu (light), Sukshma (subtle), Tikshna (penetrating), Ushna (hot), Sara (spreading), Snigdha (Uncious), Pichchila (viscid), Katu Vipaka. It also has the quality of Sugandha (aromatic), and hold Hridya (cardioprotective) property. Based on these rasa and guna, it acts as Tridosahahara (pacifies all three doshas) (Acharya YT, 2003), Kashaya Rasa (astringent in taste), Rasayana (rejuvenator), Varnya (improves complexion), Swarya (improves voice), Agnideepana (appetizer) and Ruksa (dry) paki are the additional characters mentioned by Vagbhata (Atrideva Gupt, 2005). Sushruta mentioned two types of Guggulu i.e. Naveena (Fresh) and Purana (Old) (Acharya YT, 2003). Vagbhata described acceptable characteristics for Guggulu based on its colours like Mahishaksha, Padmaraga, Kanaka, Neela, Kanaka (Atrideva Gupt, 2005). Vagbhata also gives properties of Guggulu Patra (leaves of Guggulu) as Madhura (sweet), Ruksa, Vatakaphakara, Sheeta (cold), Mala Mutra Pravataka (laxative and diuretic) and Vishtambhi (substances that cause obstruction) (Atrideva Gupt, 2005).
Synonyms

Guggulu was referred with nine different names in Brihatrayee that are reflected in Table-1. Guggulu, Palankasha and Purah are the three terms used in all the three classics. Aamisha is the term used by Sushruta, while Latvaka was clarified by Arunadatta in his commentary on Ashtanga Hridaya. Other terms like Kasara, Mahisaksha Makshika, and Rajanichara referred in Ashtanga sangraha have been clarified by Indu as Guggulu.

Categorisation

Charaka categorized it under Kashaya Skanda (category of drugs predominant in astringent taste), while Sushruta under Katu skanda (category of drugs predominant in pungent taste). Sushruta and Vagbhata both identified the drug as beneficial in Sthaulya (Obesity). Charaka and Vagbhata both grouped it under Sangyasthapana gana (group of drugs that restore consciousness). Other categories are placed at Table-2.

Guggulu as a component in different Yogas

The screening revealed that Guggulu is frequently used in different pathological conditions. It is a component of various Ghrita (medicated Ghee), Taila (medicated oil), Avaleha (confections), Choorna (powder) and Kwatha yogas. A brief of such formulations (category wise) are placed herewith.

Kwatha and Ksheera paka Yogas

Very few Kwatha yogas are found with Guggulu as a component. References are not found in Charaka Samhita, while a couple of references were found in Sushruta Samhita and Ashtanga Sangraha. One Ksheerapaka yoga (medicated milk preparation) is referred by Sushruta [Table-3].

Pana Yogas

Guggulu is preferred to administer after dissolving in suitable liquids. Gomutra is often preferred liquid media as Sahapana (Adjuvant) for Guggulu by the seers [Table-4].

Choorna Yogas

Proportion of Guggulu varies in between 1% to 12% in these choorna yogas except Krishna abhaya churna. In this formulation, Guggulu is the major constituent and conversion of the constituents into powder may be difficult [Table-5].

Leha Yogas:

Yogaraja Rasayana indicated in Kushtha, is the only Avaleha Yoga with Guggulu as a component referred by Vagbhata (Atrideva Gupt, 2005).

Taila Yogas

Total 12 Taila formulations were found with Guggulu as a component [Table-6]. In Agurvadi Taila, it is used as Kwatha dravya, while in all other formulations; it is used as Kalka (paste) dravya. All these formulations are advocated for topical application.

Table 1: Synonymous of Guggulu in Brihatrayee

<table>
<thead>
<tr>
<th>Synonymous</th>
<th>Charaka samhita</th>
<th>Sushruta samhita</th>
<th>Astanga samgraha</th>
<th>Asthanga Hridaya</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guggulu</td>
<td>+ (Sutra ¾)</td>
<td>+ (Sutra 5/18)</td>
<td>+ (Sutra 3/21)</td>
<td>+ (Sutra 14/23)</td>
</tr>
<tr>
<td>Palankasha</td>
<td>+ (Sutra 4/18)</td>
<td>+ (Uttara 31/24)</td>
<td>-</td>
<td>+ (Chikitsa 1/162)</td>
</tr>
<tr>
<td>Parah</td>
<td>+ (Vimana 8/144)</td>
<td>+ (Kalpa 5/69)</td>
<td>+ (Sutra 8/117)</td>
<td>+ (Chikitsa 1/163)</td>
</tr>
<tr>
<td>Aamisha</td>
<td>-</td>
<td>+ (Chikitsa 37/15)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Kasara</td>
<td>-</td>
<td>-</td>
<td>+ (Chikitsa 17/3)</td>
<td>-</td>
</tr>
<tr>
<td>Mahisaksha</td>
<td>-</td>
<td>-</td>
<td>+ (Uttara 33/48)</td>
<td>+ (Uttara 28/42)</td>
</tr>
<tr>
<td>Makshika</td>
<td>-</td>
<td>-</td>
<td>+ (Uttara 44/33)</td>
<td>-</td>
</tr>
<tr>
<td>Mahishakranta</td>
<td>-</td>
<td>-</td>
<td>+ (Uttara 49/178)</td>
<td>-</td>
</tr>
<tr>
<td>Rajanichara</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latvaka</td>
<td>-</td>
<td>-</td>
<td>+ (Sutra 6/93)</td>
<td></td>
</tr>
</tbody>
</table>
Table-2: Classification of Guggulu in Brihatrayee

<table>
<thead>
<tr>
<th>Text</th>
<th>Gana / Varga</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Charaka samhita</td>
<td>Sangyasthapana</td>
<td>Sutra 4/18</td>
</tr>
<tr>
<td></td>
<td>Kashaya skanda</td>
<td>Vimana 8/144</td>
</tr>
<tr>
<td></td>
<td>Pakva vrana bhedana</td>
<td>Chikitsa 25/53</td>
</tr>
<tr>
<td>Sushruta samhita</td>
<td>Sthaulyahara</td>
<td>Sutra 15/32</td>
</tr>
<tr>
<td></td>
<td>Eladi gana</td>
<td>Sutra 38/24</td>
</tr>
<tr>
<td></td>
<td>Katu varga</td>
<td>Sutra 42/11</td>
</tr>
<tr>
<td>Astanga samgraha</td>
<td>Sangyasthapana</td>
<td>Sutra 15/47</td>
</tr>
<tr>
<td></td>
<td>Sthaulyahara</td>
<td>Sutra 24/35</td>
</tr>
<tr>
<td></td>
<td>Eladi gana</td>
<td>Sutra 16/37</td>
</tr>
<tr>
<td></td>
<td>Kalmbad gana</td>
<td>Sutra 7/139</td>
</tr>
<tr>
<td></td>
<td>Danta dhavana varjya</td>
<td>Sutra 3/21</td>
</tr>
<tr>
<td></td>
<td>Agraya dravya</td>
<td>Sutra 13/3</td>
</tr>
<tr>
<td>Astanga hridaya</td>
<td>Sthaulyahara</td>
<td>Sutra 14/23</td>
</tr>
<tr>
<td></td>
<td>Eladi gana</td>
<td>Sutra 15/43</td>
</tr>
<tr>
<td></td>
<td>Kalmbad gana</td>
<td>Sutra 6/93</td>
</tr>
<tr>
<td></td>
<td>Agraya dravya</td>
<td>Uttara 40/48</td>
</tr>
</tbody>
</table>

Table-3: Kwatha and Ksheerapaka Yogas that hold Guggulu as a component

<table>
<thead>
<tr>
<th>Reference</th>
<th>Formulation</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sarivadi kwatha</td>
<td>Kaphaja jvara (Fever due to Kapha dosha)</td>
</tr>
<tr>
<td>2</td>
<td>Devadarvyadi kwatha</td>
<td>Udavarta</td>
</tr>
<tr>
<td>3</td>
<td>Sarivadi kwatha</td>
<td>Kaphaja jvara</td>
</tr>
<tr>
<td>4</td>
<td>Shodhana kashaya</td>
<td>Vrana prakshalana (wound cleanser)</td>
</tr>
<tr>
<td>Ksheerapaka Yoga</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Marichadi ksheera</td>
<td>Kasa (cough)</td>
</tr>
</tbody>
</table>

Table-4: Pana Yogas that hold Guggulu as a component

<table>
<thead>
<tr>
<th>Reference</th>
<th>Sahapana</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Gomutra (cow’s urine)</td>
<td>Udara roga (abdominal disorders)</td>
</tr>
<tr>
<td>2</td>
<td>Gomutra</td>
<td>Urustambha (stiffness in thigh muscle)</td>
</tr>
<tr>
<td>3</td>
<td>Godugdha (cow’s milk)</td>
<td>Aavrita vata</td>
</tr>
<tr>
<td>4</td>
<td>Madhu (honey)</td>
<td>Vatarakta(Gout)</td>
</tr>
<tr>
<td>5</td>
<td>Gomutra</td>
<td>Urustambha</td>
</tr>
<tr>
<td>6</td>
<td>Matra, kshara (water soluble ash), yusha, ushnodaka (warm water), dugdha</td>
<td>Gulma (abdominal lump), bhagandara (fistula in ano), krimi (worm infestation), Granthi (cyst), Shotha (inflammation), kushtha (skin disorders) etc.</td>
</tr>
<tr>
<td>7</td>
<td>Matra, kshara, ushnodaka, Yasharasana, dugdha</td>
<td>Medogata kushtha</td>
</tr>
<tr>
<td>8</td>
<td>Devadararu or shanthi kwatha</td>
<td>Medohara (anti obesity)</td>
</tr>
<tr>
<td>9</td>
<td>Matra, punarnava kwatha</td>
<td>Shotha</td>
</tr>
<tr>
<td>10</td>
<td>Matra, madhya, dugdha, kshara, draksha etc.</td>
<td>Gulma</td>
</tr>
<tr>
<td>11</td>
<td>Mahat panchamula</td>
<td>Shaulya (obesity)</td>
</tr>
</tbody>
</table>
Ashtanga Sangraha chikitsa 2/90  Shukta, gomutra, mastu  Shita jvara
Ashtanga Sangraha chikitsa 15/3  As per Rasayan prayoga  Antah vidradhi (Internal abscess)
Ashtanga Sangraha chikitsa 16/41  Gomutra or kshara & haritaki  Gulma
Ashtanga Sangraha chikitsa 19/3  Gomutra  Shotha
Ashtanga Sangraha chikitsa 21/24  As per Rasayan prayoga  Kushtha
Ashtanga Sangraha chikitsa 24/34  Dugdha  Vatarakta
Ashtanga Sangraha uttara 40/102  Madhu &Ghrita  Haritala visha (arsenic poison)
Ashtanga Sangraha uttara 49/164  Mahat panchamula, laghu panchamula, vachadi gana kwatha, mastu, ushnajala, kanji, Madya  Vata kaphaja roga (disorders of vata and kapha dosha)
Ashtanga Sangraha uttara 49/165  Varunadi gana kwatha  Badhiriya (deafness), shiro roga, meda, shwasa (dyspnea), gulma, vidradhi (abscess)
Ashtanga Sangraha uttara 49/166  Ashvagandha or jiviniya gana kwatha  Vata pitta rakta roga, Brihmana (increases body mass)
Ashtanga Sangraha uttara 49/167  Raktuachandana or padmakadi gana kwatha  Pittaja roga (diseases due to pitta dosha)
Ashtanga Sangraha uttara 49/168  Chavya, kushtha, vidanga, yavani, nagakesara, prasarani toya  Kapha vata roga
Ashtanga Sangraha uttara 49/170  Patoladi dravya kwatha  Kapha pittaja roga, shotha, visarpa (erysipelas), vrana, bhagandara, shukra, prameha (diabetes), pandu (anemia)
Ashtanga Sangraha uttara 49/172  Dugdha  Vatarakta
Ashtanga Sangraha uttara 49/173  Mansarasa, dugdha, mutra, brahmi, shankhapushpi toya  Tridoshahara
Ashtanga Hridaya sutra 14/23  Mahat panchmula  Sthaulya
Ashtanga Hridaya chikitsa 13/25  Vidradhihara kashaya  Vidradhi
Ashtanga Hridaya chikitsa 17/40  Dugdha, ardraka rasa  Udara roga
Ashtanga Hridaya chikitsa 17/49  Gomutra  Shotha
Ashtanga Hridaya chikitsa 21/49  Gomutra  Urustambha

<table>
<thead>
<tr>
<th>Reference</th>
<th>Formulation</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Charaka chikitsa 23/231</td>
<td>Sarvakamika agada</td>
<td>Pashu visha (poison of animals)</td>
</tr>
<tr>
<td>2 Charaka chikitsa 26/152</td>
<td>Pradhamanika agada</td>
<td>Pratishnya (coryza)</td>
</tr>
<tr>
<td>3 Sushruta kalpa 5/66</td>
<td>Tarkshyaya agada</td>
<td>Sarpa visha (snake poison)</td>
</tr>
<tr>
<td>4 Sushruta kalpa 5/69</td>
<td>Rashabha agada</td>
<td>Sarpa visha</td>
</tr>
<tr>
<td>5 Sushruta kalpa 6/22</td>
<td>Mahasugandhi agada</td>
<td>Sarpa visha</td>
</tr>
<tr>
<td>6 Ashtanga Sangraha chikitsa 16/15</td>
<td>Yavanyadi churna</td>
<td>Gulma</td>
</tr>
<tr>
<td>7 Ashtanga Sangraha chikitsa 17/3</td>
<td>Krishnaabha churna</td>
<td>Udara roga</td>
</tr>
<tr>
<td>8 Ashtanga Sangraha uttara 42/58</td>
<td>Tarkshyaya agada</td>
<td>Sarpa visha</td>
</tr>
</tbody>
</table>
Table-6: Taila formulations that hold Guggulu as a component

<table>
<thead>
<tr>
<th>Reference</th>
<th>Formulation</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Charaka chikitsa 3/267</td>
<td>Agurvadi taila</td>
<td>Shita jvara (fever with chills)</td>
</tr>
<tr>
<td>2 Charaka chikitsa 10/34</td>
<td>Palanksha taila</td>
<td>Apasmara (epilepsy)</td>
</tr>
<tr>
<td>3 Ashtanga Sangraha chikitsa 2/90</td>
<td>Tagaradi taila</td>
<td>Shita jvara</td>
</tr>
<tr>
<td>4 Ashtanga Hridaya chikitsa 12/40</td>
<td>Vranaropaka taila</td>
<td>Premeha pidika (diabetic carbuncle)</td>
</tr>
<tr>
<td>5 Ashtanga Sangraha chikitsa 21/67</td>
<td>Mahavajra taila</td>
<td>Kashtha</td>
</tr>
<tr>
<td>6 Ashtanga Sangraha chikitsa 21/69</td>
<td>Sikthakadi taila</td>
<td>Kashtha</td>
</tr>
<tr>
<td>7 Ashtanga Sangraha uttara 6/17</td>
<td>Guggulvadi taila</td>
<td>Graha</td>
</tr>
<tr>
<td>8 Ashtanga Sangraha uttara 6/27</td>
<td>Lakshmyadi taila</td>
<td>Graha</td>
</tr>
<tr>
<td>9 Ashtanga Sangraha uttara 10/31</td>
<td>Palankashadi taila</td>
<td>Apasmara</td>
</tr>
<tr>
<td>10 Ashtanga Hridaya chikitsa 19/81</td>
<td>Mahavajraka taila</td>
<td>Kashtha</td>
</tr>
<tr>
<td>11 Ashtanga Hridaya chikitsa 19/84</td>
<td>Sikthakadi taila</td>
<td>Vicharchika (eczema)</td>
</tr>
<tr>
<td>12 Ashtanga Hridaya uttara 22/3</td>
<td>Mahusnehadhi taila</td>
<td>Oshita roga (diseases in lips)</td>
</tr>
</tbody>
</table>

Ghrita Yogas

Total 13 Ghrita (Ghee) based formulations were found with Guggulu as an ingredient [Table-7]. In majority of formulations, Guggulu is used as Kalka dravya. Except Baladi Ghrita of Charaka, all other formulations are advocated for internal administration.

Sandhana Yogas

Sandhana yogas (self generated alcoholic preparations) with Guggulu as a component are not found in Charaka Samhita or Sushruta Samhita. A few formulations were referred by Vagbhata [Table-8].

Lepa Yogas

These formulations of Guggulu are indicated for topical application as wound healers, wound cleansing agents etc. They were equally used in different skin diseases [Table-9].

Table-7: Ghrita formulations that hold Guggulu as a component

<table>
<thead>
<tr>
<th>Reference</th>
<th>Formulation</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Charaka chikitsa 8/78</td>
<td>Baladi ghrita</td>
<td>Shirahshool (Headache)</td>
</tr>
<tr>
<td>2 Charaka chikitsa 9/46</td>
<td>Mahapaishachika ghrita</td>
<td>Unmada (psychosis)</td>
</tr>
<tr>
<td>3 Charaka chikitsa 10/27</td>
<td>Vachadi grita</td>
<td>Apasmara</td>
</tr>
<tr>
<td>4 Sushruta uttara 61/27</td>
<td>Kutilhadi grita</td>
<td>Apasmara</td>
</tr>
<tr>
<td>5 Sushruta chikitsa 7/14</td>
<td>Varunadi grita</td>
<td>Ashmari (calculus)</td>
</tr>
<tr>
<td>6 Ashtanga Sangraha chikitsa 6/67</td>
<td>Puradi ghrita</td>
<td>Swasa</td>
</tr>
<tr>
<td>7 Ashtanga Sangraha chikitsa 13/14</td>
<td>Varunadi ghrita</td>
<td>Ashmari</td>
</tr>
<tr>
<td>8 Ashtanga Sangraha chikitsa 21/6</td>
<td>Panchikta ghrita Guggulu</td>
<td>Kushtha</td>
</tr>
<tr>
<td>9 Ashtanga Sangraha chikitsa 23/35</td>
<td>Panchikta ghrita Guggulu</td>
<td>Vatavyadhi (neurological disorders)</td>
</tr>
<tr>
<td>10 Ashtanga Sangraha uttara 9/21</td>
<td>Mahapaishachika ghrita</td>
<td>Unmanda</td>
</tr>
<tr>
<td>11 Ashtanga Sangraha uttara 49/157</td>
<td>Martyamrita ghrita</td>
<td>Rasayana (rejuvenator)</td>
</tr>
<tr>
<td>12 Ashtanga Hridaya chikitsa 11/25</td>
<td>Varunadi ghrita</td>
<td>Ashmari</td>
</tr>
<tr>
<td>13 Ashtanga Hridaya chikitsa 21/60</td>
<td>Nimbadi ghrita</td>
<td>Vatavyadhi</td>
</tr>
</tbody>
</table>

Table-8: Sandhana Yogas that hold Guggulu as a component

<table>
<thead>
<tr>
<th>Reference</th>
<th>Formulation</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Ashtanga Sangraha chikitsa 10/23</td>
<td>Guggulasava</td>
<td>Arsha (piles)</td>
</tr>
<tr>
<td>2 Ashtanga Sangraha chikitsa 21/24</td>
<td>Guggulasava</td>
<td>Kastha</td>
</tr>
<tr>
<td>3 Ashtanga Hridaya chikitsa 8/146</td>
<td>Putikaranja chukra</td>
<td>Arsha</td>
</tr>
</tbody>
</table>
Table-9: Lepa Yogas that hold Guggulu as a component

<table>
<thead>
<tr>
<th>Reference</th>
<th>Indication</th>
<th>Liquid media</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Charaka Sutra ¾</td>
<td>Kushtha</td>
</tr>
<tr>
<td>2</td>
<td>Charaka chikitsa 8/78</td>
<td>Shira shoola</td>
</tr>
<tr>
<td>3</td>
<td>Charaka chikitsa 25/53</td>
<td>Pakya vrana bhedana</td>
</tr>
<tr>
<td>4</td>
<td>Charaka chikitsa 25/100</td>
<td>Vrana avasadana karma</td>
</tr>
<tr>
<td>5</td>
<td>Sushruta chikitsa 22/5</td>
<td>Pratisarana Dravya</td>
</tr>
<tr>
<td>6</td>
<td>Sushruta kalpa 8/137</td>
<td>Mushaka visha</td>
</tr>
<tr>
<td>7</td>
<td>Ashtanga Sangraha sutra 11/31</td>
<td>Alasaka (intestinal atony)</td>
</tr>
<tr>
<td>8</td>
<td>Ashtanga Sangraha chikitsa 7/98</td>
<td>Rajyakshma (tuberculosis)</td>
</tr>
<tr>
<td>9</td>
<td>Ashtanga Sangraha chikitsa 21/57</td>
<td>Vrana</td>
</tr>
<tr>
<td>10</td>
<td>Ashtanga Sangraha chikitsa 21/62</td>
<td>Vrana</td>
</tr>
<tr>
<td>11</td>
<td>Ashtanga Sangraha uttara 6/2</td>
<td>Skanda Graha</td>
</tr>
<tr>
<td>12</td>
<td>Ashtanga Sangraha uttara 6/24</td>
<td>Pitru graham</td>
</tr>
<tr>
<td>13</td>
<td>Ashtanga Sangraha uttara 6/27</td>
<td>Pitru graham</td>
</tr>
<tr>
<td>14</td>
<td>Ashtanga Sangraha uttara 30/29</td>
<td>Vrana</td>
</tr>
<tr>
<td>15</td>
<td>Ashtanga Sangraha uttara 30/47</td>
<td>Avasadana Karma</td>
</tr>
<tr>
<td>16</td>
<td>Ashtanga Sangraha uttara 40/78</td>
<td>Vrana</td>
</tr>
<tr>
<td>17</td>
<td>Ashtanga Sangraha uttara 42/62</td>
<td>Vrana</td>
</tr>
<tr>
<td>18</td>
<td>Ashtanga Sangraha uttara 44/54</td>
<td>Lata karnika patina</td>
</tr>
<tr>
<td>19</td>
<td>Ashtanga Sangraha uttara 46/53</td>
<td>Alarka visha</td>
</tr>
<tr>
<td>20</td>
<td>Ashtanga Sangraha uttara 49/171</td>
<td>Galaroga</td>
</tr>
<tr>
<td>21</td>
<td>Ashtanga Hridaya chikitsa 19/71</td>
<td>Vrana</td>
</tr>
<tr>
<td>22</td>
<td>Ashtanga Hridaya uttara 25/37</td>
<td>Vrana darana</td>
</tr>
<tr>
<td>23</td>
<td>Ashtanga Hridaya uttara 25/49</td>
<td>Vrana avasadana</td>
</tr>
</tbody>
</table>

Dhoopana Yogas

As Guggulu has rakshoghna activity, it was often preferred as a component in dhoopana (fumigation) yogas. It is used in conditions like Vrana (wound), karna puya (pus discharge from ear), visha vrana (wound due to poison), vishama jvara (intermittent fever), shwasa, yoni roga (vaginal diseases), mukharoga (diseases of oral cavity) etc. These formulations are also preferred as preventive aspects like in Bala Rakshakarma (measures that protect a neonate from infection), Vrana Paschat karma (post operative measures of wound), Prayogika Dhoomapana etc. [Table 10].

Other solid forms

A few references of solid dosage forms were found in classics where Guggulu is found to be the major constituent. All these references are referred by Vagbhata, except one by Charaka [Table 11].

Table-10: Dhoopana Yogas that hold Guggulu as a component

<table>
<thead>
<tr>
<th>Reference</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Charaka sutra 5/21</td>
</tr>
<tr>
<td>2</td>
<td>Charaka sharira 8/61</td>
</tr>
<tr>
<td>3</td>
<td>Charaka chikitsa 3/307</td>
</tr>
<tr>
<td>4</td>
<td>Charaka chikitsa 17/80</td>
</tr>
<tr>
<td>5</td>
<td>Charaka chikitsa 23/100</td>
</tr>
<tr>
<td>6</td>
<td>Charaka chikitsa 26/182</td>
</tr>
<tr>
<td>7</td>
<td>Charaka chikitsa 30/121</td>
</tr>
<tr>
<td>8</td>
<td>Sushruta sutra 5/18</td>
</tr>
<tr>
<td>9</td>
<td>Sushruta chikitsa 22/69</td>
</tr>
<tr>
<td>10</td>
<td>Sushruta chikitsa 40/4</td>
</tr>
</tbody>
</table>
DISCUSSION:

Charaka categorized Guggulu under Kashaya Skandha, while Sushruta under Katu Skandha. This may be due to differences in approaches of drug classification. Guggulu is katu rasa dominant drug, but the activities are similar assigned to kashaya rasa. Therefore the classification of Guggulu by both seers can be considered as equivalent. Sushruta and Vagbhata grouped the drug under Eladi Gana.

<table>
<thead>
<tr>
<th>References</th>
<th>Formulation</th>
<th>Guggulu %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Charaka kalpa 1/23</td>
<td>Modaka/Utkarika</td>
</tr>
<tr>
<td>2</td>
<td>Astanga sangraha kalpa 1/13</td>
<td>Modaka</td>
</tr>
<tr>
<td>3</td>
<td>Astanga sangraha uttara 33/45</td>
<td>Amritadi Guggulu</td>
</tr>
<tr>
<td>4</td>
<td>Astanga sangraha uttara 33/46</td>
<td>Swayambhu Guggulu</td>
</tr>
<tr>
<td>5</td>
<td>Astanga sangraha uttara.33/48</td>
<td>Uttamadi Guggulu</td>
</tr>
<tr>
<td>6</td>
<td>Astanga sangraha uttara.49/169</td>
<td>Trayushanadi Guggulu</td>
</tr>
<tr>
<td>7</td>
<td>Astanga sangraha uttara 49/174</td>
<td>Magadhikadi Guggulu</td>
</tr>
<tr>
<td>8</td>
<td>Ashtanga hridaya chikitsa 21/50</td>
<td>Vyoshadi Guggulu</td>
</tr>
<tr>
<td>9</td>
<td>Ashtanga hridaya uttara 28/38</td>
<td>Amrutadi Guggulu</td>
</tr>
<tr>
<td>10</td>
<td>Ashtanga hridaya uttara 28/39</td>
<td>Magadhikadi Guggulu</td>
</tr>
<tr>
<td>11</td>
<td>Ashtanga hridaya uttara 28/40</td>
<td>Swayambhu Guggulu</td>
</tr>
<tr>
<td>12</td>
<td>Ashtanga hridaya uttara 28/42</td>
<td>Uttamadi yoga</td>
</tr>
</tbody>
</table>

Table-11: Other solid forms that hold Guggulu as a component
The drugs of this group are aromatic in nature and preferred for Varna prasadana and Vata kaphahara purposes.

A specific classification of Guggulu is not found in any of the Brihatrayee except a brief description on acceptable qualities mentioned by Vaghbata. Possibly, these qualities have been considered by later seers like Bhavamishra to describe the types of Guggulu.

Guggulu formulations are being used often in various disease conditions. In the current study, an attempt has been made through brihatrayee to know different forms of Guggulu preferred in those days. Screening revealed that seers rarely preferred using Guggulu as a major component in formulations. They often dispensed it in the form of Pana (33), Ghrita (13), Taila (12), Choornna (8), Sandhana (3), Avaleha (1), and Kwatha yogas (5). Majority of the formulations with Guggulu as a component are preferred as Dhooma yogas (40) and Lepas (23). Rakshoghna (preventive), krimighna (anti-parasitic), bhootaghna karma (anti-microbial) of Guggulu will be beneficial in such forms that will help in would healing, disinfecting, anti-microbial etc. Lekhana (scraping) property of Guggulu is also beneficial in checking the pathologies at localized lesions. Guggulu possess significant antimicrobial properties as an individual component and in combinations like Triphala Guggulu (Sejal Patel et al., 2012). The essential oil, chloroform extract and sesquiterpenoids isolated from the oleo-gum-resin of Guggulu also possess inhibiting activity against both Gram (+) and Gram (−) bacteria (Saeed M A et al., 2004). Fumigation of Guggulu gum also showed considerable decrease in concentration of fungal load and found useful to curtail the concentration of fungi like Aspergillus, Penicillium, Alternaria, Curvularia, Cladosporium etc (Rashmi Tewary et al., 1997). The drug also has an ability to promote synthesis of intracellular triglycerides and reduces depth of large and small wrinkles, thus giving the skin a smooth appearance (Andre et al., 1999). Hence topical applications will smoothen the skin besides checking the pathology.

Most of the Ghrita preparations were advocated for internal purposes, while Taila preparations are preferred as topical applications in cases of Prameha pidika, Vicharchika, Kushtha etc. Churnas with Guggulu were preferred in both external and internal routes. Guggulu was dispersed with kwatha or other suitable liquids in many diseases. These formulations are mainly used in Aamajanya koshtha vyadhi (different forms of Gastro Intestinal disorders).

Alodhana (mixing with liquids) is preferred in many Pana yogas (medicated beverages) of internal administration. It specifies that, Guggulu was preferred to be dissolved completely in suitable liquids before its consumption. These liquid medias change with status of the doshas or condition of the diseases. For example, Guggulu should be dissolved in Gomutra to use in shotha, udara, urustambha and gulma etc conditions. Guggulu dissolved in dugdha (milk) is indicated in vatarakta.

Some solid dosage forms are also found in samhitas. Charaka referred Modaka or Utkarika for Virechana (purgative) that holds Guggulu as an ingredient. But, the proportion of Guggulu in this formulation is very less (~5%). Ashtanga Samgraha and Ashtanga Hridaya also hold few formulations that contain 50% of Guggulu (Pandit B.H. et al., 2005). It is quite interesting to note that all these formulations are explained in one chapter and advised to consume with honey. These combinations will attain solid form and can be grouped under Vati or Modaka Kalpana. Indu, at places preferred converting the formulation into pindikrutam, equivalent to pill dosage form (Atrideva Gupta, 2005). As the Commentator belongs to 13th AD; possibly he observed the pharmaceutical developments and advised converting the combination into pills.
CONCLUSION:

As *Guggulu* has good binding capacity, the pills thus developed will have a greater disintegration time (Anjana Chaube *et al.*, 1995) and at times may not get disintegrated in stomach leading to its inactivity. Considering this; the physicians of current scenario advice crushing of *Guggulu* pills before their swallowing for proper assimilation and absorption. Possibly considering this in view; the seers of ancient time had advised dissolving *Guggulu* completely in suitable liquids before its consumption as evident in current screening. The solid forms of *Guggulu* in these three classics were preferred as *varti* or *lepa* or for *dhooma* purposes. This screening also makes clear that conversion of *Guggulu* into *vati* form has entered into the field of therapeutics after 7th AD.

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