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"STUDY OF PHARMACOLOGICAL ACTIVITIES OF BEHADA : A REVIEW"

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ABSTRACT

In traditional Indian Ayurvedic medicine, Beleric is known as "Bibhitaki" (Marathi: "Behada or Bhenda") (Terminalia bellirica). Its fruit is used in the popular Indian herbal rasayana treatment triphala. In Sanskrit it is called bibhītaka. In India, Neemuch; a town in Malwa Region of Madhya Pradesh is a major trading centre of skinless baheda and entire fruits of T. bellirica. The fruits are widely collected in the wild in the Malwa region of Madhya Pradesh.

KEYWORDS: *Antioxidant, anticancer, inflammation, antimicrobial, diabetes and medicinal plants.*

INTRODUCTION

Plants have a long history of usage as therapeutic agents and were the main source of medicines prior to the advances of modern medicine. In many developing countries, 3 herbal medicinal systems remain important in the treatment of many ailments. Ayuvedic medicine is still commonly practiced within India with an estimated 85% of Indians still using crude plant preparations for the treatment of a wide variety of diseases and ailments (Kamboj, 2000). Traditional Chinese medicine (TCM) and African medicinal systems also account for a major portion of health care in their populations. Even in countries where allopathic/Western medicine is dominant, much is also owed to plant medicinal systems. Furthermore, many users are returning to herbal medicinal systems due to the perception that natural medicines are often a safer alternative than allopathic drugs, as well as seeking treatments for diseases which modern medicine does not yet have solutions.

Many of the prescription drugs currently marketed for a wide variety of ailments were originally isolated from plants and/or are semi-synthetic analogues of phytochemicals. It has been estimated that approximately 25% of all prescription drugs currently in use are of plant origin (Walsh, 2003; Newman and Cragg, 2007). Furthermore, approximately 75% of new anticancer drugs marketed between 1981 and 2006 were derived from plant compounds (Newman and Cragg, 2007). Traditionally, plant based medicines have been used as crude formulations such as infusions, tinctures and extracts, essential oils, powders, poultices and other herbal preparations. The current trend is to isolate and characterise the individual phytochemical components with the aim of producing an analogue of increased bioactivity/bioavailability. Such studies have given rise to many useful drugs such as quinine (from Cinchona spp.) and digoxin (from Digitalis spp.) as well as the anticancer drugs vincristine and vinblastine (from Vinca rosea). However, the bioactivities seen for crude extracts are often much enhanced, or even totally different to those seen for the individual components (Karalliedde and Gawarammana, 2008; Choi and Chung, 2003). Crude plant extracts may contain hundreds, or even

thousands of different chemical constituents that interact in complex ways. Often it is not known how an extract works, even when its therapeutic benefit is well established.

The genus Terminalia (Family Combretaceae) comprises approximately 200-250 species of medium to large flowering trees, many of which have a history of usage in traditional medicinal systems (McGaw et al, 2001). Terminalia species are widely distributed through the tropical and subtropical regions of Asia, Australia and Africa. 4 With arguably the greatest number and diversity, the Asian Terminalia's cover many of the most useful species with the most extensive documentation of their therapeutic effects. Asian Terminalia species are widespread, occurring from the Malaysian peninsula and the Indonesian archipelago in the east, across Southern Asia to Western Asia and into the Middle East. The biology of many of these species are especially well studied due to their usage in a variety of Asian medicinal systems. Of the species that are native to Asia, Terminalia arjuna and Terminalia chebula are particularly well documented due to their myriad of uses in Ayuverdic medicine. Approximately 28 species are known to occur in Australia and the South Pacific region. Of these, Terminalia ferdinandiana has been receiving recent attention due to its interesting phytochemistry and its high antioxidant content/activity. A further 30 species approximately occur in Africa, with the majority of these occurring in the southern part of the continent. A number of Terminalia species are also native to the North, Central and South America.

The bark of many Terminalia species is often fissured and the branches are arranged in tiers. The genus name is derived from the Latin word terminus, referring to the fact that the leaves are located at the very tips of the shoots. Leaves of most species of Terminalia are usually large and have a leathery feel. The small (usually) greenishwhite flowers appear on spikes or in clusters. Fruit may be yellow, dark red or black drupes which are usually angled or winged. The fruit from some plants is edible and may in fact be highly nutritious.

Synonyms :

- Assam - Bhomora, Bhomra, Bhaira;
- Eng – Beleric Myrobalan;
- Guj - Bahedam, Baheda;
- Hindi - Bahera;
- Kan - Shanti, Shantikayi, Tare, Tarekayi;
- Mal - Tanni, Tannikai;
- Mar - Baheda;
- Ori - Baheda, Bhara;
- Sansk - Vibhita, Aksa, Aksaka, Bibhitaki;
- Tam - Thanakkai, Tanri, tanrikkai, Tani;
- Tel - Tannikkaya, Vibhitakami, Tani

Plant description:

Terminalia bellerica is a large deciduous tree to 50 m tall and a diameter of 3 m with a rounded crown. The frequently buttressed bole at the base is branchless up to 20 m. The bark is bluish or ashy-grey covered with numerous fine longitudinal cracks, the inner bark yellowish. Leaves large, glabrous, alternate, broadly elliptic to obovate-elliptical, 4-24 cm x 2-11 cm, base rounded to cuneate, rufous-sericeous but soon glabrescent, with 6-9 pairs of secondary veins. Secondary and tertiary venation prominent on both surfaces, clustered towards the ends of branchlets. Petiole 2.5-9 cm long. Young leaves copper-red, soon becoming parrot green, then dark green. Flowers solitary, small, 3-15 cm long, greenish white, simple, axillary spikes; calyx tube densely sericeous or tomentulose; flowers appear along with new leaves and have a strong honey-like smell. Fruit sub-globular to broadly ellipsoid, 2-4 x 1.8-2.2 cm, densely velutinous or sericeous, light-yellow, obscurely 5-angled and minutely brown tomentosa. The generic name 'Terminalia' comes from Latin word 'terminus' or 'terminalis' (ending), and refers to the habit of the leaves being crowded or borne on the tips of the shoots.

DISCUSSION:

Traditional uses : Fruits are laxative, astringent, anthelmintic and antipyretic; useful in hepatitis, bronchitis, asthma, dyspepsia, piles, diarrhoea, coughs, hoarseness of voice, eye diseases and scorpion-sting; used as a hair tonic. Decoction of the green fruit is used for cough. Pulp of the fruit is useful in dysenteric-diarrhoea, dropsy, piles and leprosy. Half ripe fruit is used as purgative. Kernel of the fruit is narcotic. Fruits are used in menstrual disorder in Khagrachari. Seed oil is used in rheumatism. Gum of the bark is demulcent and purgative. The triterpenoid present in the fruits possess significant antimicrobial activity. Kernel oil has purgative action and its prolonged use was well tolerated in mice (Ghani, 2003).

Phytoconstituents: Glucoside (bellericanin), Gallo-tannic acid, Coloring matter, resins and a greenish yellow oil. Ellagic acid, gallic acid, lignans (termilignan and thannilignan), 7- hydroxy 3'4' (methylenedioxy) flavone and anolignanB. Tannins, ellagic acid, ethyl gallate, galloyl glucose and chebulagic acid, phyllemblin, β-sitosterol, mannitol, glucose, fructose and rhamnose .

PHARMACOLOGICAL EFFECTS :

Analgesic activity: ArifUllah Khan et al., (2010) describes the antisecretory and analgesic activities of the crude extract of Terminalia bellerica. T. bellerica extract at the dose range of 300 - 1000 mg/kg inhibited the castor oilinduced intestinal fluid secretion in mice. The extract also dose-dependently (50 - 100 mg/kg) where it reduced the numbers of acetic acid-mediated in mice. These results indicate that TB exhibit antisecretory and antinociceptive effects, hence justifying its medicinal use in diarrhea and pain.

Anti diarrhoeal activity: The Anti diarrhoeal activity was performed using Castor oil induced diarrhoea, PGE2 induced entero pooling and gastrointestinal motility test (Bimlesh Kumar et al., 2010). Aqueous and ethanolic extract of fruit pulp of TB at the doses of 334 mg/kg, 200 mg/kg, 143 mg/kg were used. Comparison of percentage protection in these models revealed that the extracts have more prominent anti-secretory effect than the reduction in gastrointestinal motility.

Antihypertensive Effect: Arif Ullah Khan et al., (2008) was screened the effect of TB in hypertension. After administration of TB, they observed that fall in the arterial BP of rats under anaesthesia. In isolated guinea-pig atria, inhibition of force and rate of atrial contractions noted. In rabbit thoracic aorta, relaxation was observed after the induction of contractions which was induced by phenylephrine.

Anti salmonella activity: Madani A et al., (2008) were studied the effect of T. belerica against Salmonella typhi and Salmonella typhimurium. In vitro cellular toxicity also performed by them. In this study, Petroleum ether, chloroform, acetone, alcohol and aqueous extract of TB fruit taken for screening. When compared with other extracts bothalcoholic and aqueous extracts of TB showed significant anti-salmonella activity. There was no cytotoxicity was observed in in vitro cellular toxicity study.

Anti-Spasmodic and Bronchodilatory Properties: Anwarul Hassan Gilani et al., (2008) were postulated that the crude extract of TB fruits elicited relaxation of spontaneous contractions in both isolated rabbit jejunum and guinea-pig ileum. Protective effect of TB against castor oil-induced diarrhea and carbachol-mediated bronchoconstriction also observed in rodents. In guinea-pig trachea, TB relaxed the CCh-induced contractions.

Anti-microbial activity: Elizabeth K M et al., (2005) were conducted the antimicrobial activity of TB against 9 human microbial pathogens. The Aqueous extract of dry fruit at 4 mg concentration showed highest zone of inhibition against S.aureus. These pathogens were highly sensitive to the methanol extract also except E. coli (enteropathogen) and P. aeruginosa. Finally they concluded that TB dry fruit possesses potential broad spectrum antimicrobial activity.

Antimicrobial and Toxicity Studies: Badrul Alam et al., (2011) postulated that the crude methanolic extract of the fruits of Terminalia belerica Roxb along with its various organic fractions elicited both in vitro and in vivo antioxidant activity as well as antibacterial activity. Total antioxidant activity, scavenging free radical, authentic peroxynitrite and reducing power assessment were performed.

Finally they concluded that the EtOAc fraction elicited strong activity in all the model systems with moderate toxicity.

Antioxidant activity: Ramesh Kumar et al., (2011) postulated that the crude aqueous extract of the fruits of Terminalia belerica Roxb have antioxidant properties since these contains enzymatic and non – enzymatic antioxidants, these can be very effective against microbes causing various diseases. In vitro assessment of the antioxidant activity of ethanolic fractions of both these plants to scavenge 2, 2-Diphenyl-1-picrylhydrazyl (DPPH) and highly reactive hydroxyl radicals showed that the semi pure compounds present in the fractions are useful potential source of antioxidants and can be used in the therapy of diseases like cancer, coronary heart disease, ageing and any other disease related to oxidative stress. These fractions being non-toxic showed significant antioxidant activity at scavenging free radicals. They also significantly scavenge hydroxyl radical which is known to cause cellular damage.

Wound healing activity: Saha et al. (2011) postulated that the paste of Terminalia belerica Roxb have proper efficacy on wound healing. Herbal paste preparation showed significant (P< 1) for P. emblica/doxorubicin or cisplatin at different dose levels were demonstrated in A549 and HepG2 cells. The T. bellerica/cisplatin or doxorubicin also showed synergistic effects in A549 and HepG2 cells. In some instances, the combinations resulted in antagonistic effects. The dose reduction level was different and specific to each combination and cell line.

Immunological activity: Aurasorn Saraphan choti witthaya et al. postulated that T. bellerica extract affected T cell proliferation mainly through the same mechanism as PHA. The extract with LPS and PWM also affected B cell proliferation through T cell-independent and T celldependent mechanisms respectively. The results indicated that the extract affected cellular mediated immunity (CMI) rather than humoral mediated immunity (HMI).

Acute and Sub-acute Toxicities: Thanabhorn S. et al., (2009) were conducted acute and sub-acute toxicity studies as per the OECD guideline. Single oral administration of the ethanolic extract of T. belerica at a dose of 5,000 mg/kg did not produce any toxicity. In sub-acute toxicity, repeated administration of 1,000 mg/kg of T. belerica over 14 days did not cause changes in terms of general behaviors, mortality, weight gain, hematological or clinical blood chemistry parameters. The results of histological examinations showed normal appearance of the internal organs when compared to those of the control group.

Immune response In vitro: In vitro Phagocytic activity and lymphocyte proliferation assay were carried out in methanolic extract of on the mouse immune system (Aurasorn Saraphanchotiwitthaya et al., 2008). In both assay, stimulation of macrophage phagocytosis and maximal activation of phytohemagglutinin were observed. Finally, the authors concluded that the methanolic extract of T. belerica affected the mouse immune system, specifically both the cellular and humoral immune response in vitro.

Hepatoprotective activity: Sangeetha Shukla et al, (2006) were evaluated the protective effect of TB fruit extract and its active principle, Gallic acid against CCl4 intoxication. Treatment with extract (200, 400 and 800 mg/kg, p.o.) and gallic acid (50, 100 and 200 mg/kg, p.o.) showed dose-dependent recovery in biochemical parameters such as SGOT, SGPT and lipid peroxidase, glutathione but the effect was more pronounced with gallic acid.

Antibiofilm Activity: The ethanolic extract of a plant Terminalia bellerica (common name = Baheda) was tested for its antimicrobial activity against the oral plaque forming bacteria Streptococcus mutans. It was found to significantly inhibit biofilm formation. It was found that the extract from Terminalia bellerica showed strong activity against Streptococcus mutans. The extract also prevents the formation of biofilm by the bacteria. The study suggests possible benefits of this herbal preparation which inhibit the biofilm formation by streptococci, a oral pathogens.

Anticancer Activity: P. emblica and T. bellerica extracts demonstrated growth inhibitory activity, with a certain degree of selectivity against the two cancer cell lines tested. Synergistic effects (CI < 1) for P. emblica/doxorubicin or cisplatin at different dose levels were demonstrated in A549 and HepG2 cells. The T. bellerica/cisplatin or doxorubicin also showed synergistic effects in A549 and HepG2 cells. In

some instances, the combinations resulted in antagonistic effects. The dose reduction level was different and specific to each combination and cell line.

β-lactamase inhibitor activity: The β-lactamase inhibitor activity of 68 extracts from Indian herbs and spices was surveyed. Most promising results of the β-lactamase inhibitor activity invivo and in vitro were achieved from the herbal extracts of Baheda (Terminalia bellerica), Ginger (Zingiber officinale), Brahmi (Bacopa monnieri), Garlic (Allium sativum), Gurmar (Gymnema sylvestre), Satavar (Asparagus racemosus) and Pomegranate (Punica granatum) peels and seeds against Staphylococcus aureus as the test organism.

Antiulcer Activity: The anti-ulcer activity of ethanolic extract of Terminalia belerica (Combretaceae) fruits ETB was investigated in pylorus ligation and ethanol induced ulcer models in wistar rats. In both models the common parameter determined was ulcer index. ETB at doses of 250,500 mg/kg orally produced significant inhibition of the gastric lesions induced by Pylorus ligation induced ulcer & Ethanol induced gastric ulcer.

Antithrombotic and Thrombolytic activity: An in vitro model was used to check the clot lysis and antithrombotic effect of Terminalia belerica fruits along with Streptokinase as a positive control. From this study it was found that after addition of Streptokinase clot formation is delayed upto more than 90 min whereas after addition of test solution it was found that as the concentration of extract was increased the delay in clot formation also increases. At 0.20 mg/dl concentration it showed the maximum delay (more than 90 min.) in clot formation. For thrombolytic activity, at concentration 1.00 mg/dl the clot dissolution time is minimum i.e. 58 and 66 min for aqueous and alcoholic extracts respectively.

Antipyretic Activity: The antipyretic activity of ethanolic and aqueous extracts of Terminalia bellirica fruits (200 mg/kg, p.o.) was studied in brewer's yeast-induced fever models in mice and rats. Both extracts showed a significant inhibition of elevated body temperature when compared to corresponding control.

Antimutagenic Activity: Water, acetone, and chloroform extracts of Terminalia bellerica were examined for their antimutagenic potency using the Ames Salmonella/microsome assay. Acetone extract exhibited variable inhibitory activity of 65.6%, and 69.7% with 4-Onitrophenylenediamine (NPD) and sodium azide, respectively (as direct-acting mutagens), and 81.4% with 2- aminofluorene (2AF) (an S9-dependent mutagen), in the preincubation mode of experimentation. Inhibition with chloroform and water extracts was rather insignificant.

CONCLUSION:

Medicinal plants have been identified and used throughout human history. The study of traditional human uses of plants, is recognized as an effective way to discover future medicines. The use of herbs to treat diseases is almost universal among non- industrialized societies and is often more affordable than purchasing modern pharmaceuticals. Crude extracts of various parts of Terminalia bellerica plant have been found to contain constituents such as Glucoside, Gallo-tannic acid, colouring matter, resins and agreenish yellow oil. Ellagic acid, gallic acid, lignans, 7-hydroxy 3'4' flavone and anolignan B. Tannins, ellagic acid, ethyl gallate, galloyl glucose and chebulic acid, phyllemblin, β-sitosterol mannitol, glucose, fructose and rhamnose. These compounds are believed to be responsible for the pharmacological activities such as antimicrobial, antioxidant, antisalmonella, hepatoprotective, antispasmodic and bronchodilatory activities. Therefore, this plant is significantly used for the treatment and prevention of diseases. Further studies should be carried out for this plant to discover the unrevealed part of it which may serve for the welfare of mankind.

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