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A REVIEW ON BALADUR (*SEMECARPUS ANACARDIUM*): ANUNANI MEDICINAL PLANT HAVING NUMEROUSPHARMACOLOGICALPROPERTIES

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ABSTRACT

Hepatocellular carcinoma (HCC) is the world's seventh most common cancer and the third leading cause of mortality. Herbal drugs are important in health, especially in remote areas of developing countries with few healthcare facilities. Several studies have found that using medicinal plants to treat infectious and non-infectious diseases is effective. In India, hepatocellular carcinoma is a common complication of chronic liver disease. Primary liver cancer is the sixth most common cancer in the world and the fourth leading cause of cancer death. As a result, more research into the tumor cycle and its prevention through appropriate herbal (Unani/Ayurvedic) medication are critical to mitigating the deadly disease's effects. According to WHO estimates, approximately three-quarters of the world's population now uses herbs or traditional medicines to treat a variety of ailments, including liver diseases.Animal models and liver cancer cell lines are used to investigate the treatment efficacy against various chemically induced liver damage.Antioxidants derived from medicinal plants and common dietary sources can protect the liver from damage caused by chemicals and the oxidative stress mechanism.We conducted a comprehensive literature review to determine the role of various herbs with liver protective and antioxidant properties, and the results are presented here. This data will be useful to researchers working on liver carcinoma and free radical scavenging, both of which are significant in removing potential carcinogens.

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INTRODUCTION

A glandular organ of the digestive system is the liver. It plays a complicated part in the body's metabolism. There is evidence linking the liver to more than 100 essential physiological functions.Some of its important functions include metabolic pathway regulation, glycogen storage, hormone secretion, protein synthesis, detoxification, digestion, and RBC decomposition. [1]Hepatocellular carcinoma (HCC) is the world's third most common cause of cancer death currently Each year, this cancer is diagnosed in much more than 800,000 people globally. Despite its massive global impact, there is considerable disagreement about how to stage and characterize this cancer. [2]The different approaches to treating HCC are partly a result of cancer's inherent clinical and biologic heterogeneity, but they are also a result of how doctors and clinical researchers see the disease.[3]Pathological processes that lead to various chronic liver diseases include the progressive destruction and regeneration of liver parenchyma. Among the most common chronic liver diseases are viral hepatitis, alcoholic or non-alcoholic fatty liver disease, autoimmune hepatitis, cirrhosis, and hepatocellular carcinoma.[4]

Most of the cells either die or convert to a fibrotic condition in severe liver damage situations. In these circumstances, the therapy options include some therapeutic medicines as well as some agents that can encourage the growth of liver cells.Because they are more readily available, human liver cell lines either from malignant tissue or created by genetic engineering of primary liver cells are frequently used in *In vitro* research.These cells are suitable for in vitro research under repeatable and standardized conditions due to their stable metabolism and higher proliferative potential. Most *In vitro* research for the creation of cancer therapies uses the hepatoma cell line HepG2.According to reports, cell lines are crucial for studying metabolic pathways or testing potential drugs alone or in combination to treat cancer.[5], [6]

The primary causes are excessive alcohol consumption, virus infection, obesity, diabetes, and drug-induced liver damage. Chronic liver diseases kill between 3.9 and 6.9 humans per 100,000 in different parts of the world. [7]Since antiquity, plants have been a source of a large number of medicinal compounds that have played a dominant role in the maintenance of human health. Over half of all modern clinical drugs are naturally derived, and natural products play an important role in pharmaceutical drug development. [8]In India, chronic liver diseases frequently progress to hepatocellular carcinoma. Every year, approximately 22,000 new cases of primary liver cancer are reported in the country. Secondary liver cancer is about twenty times more common than primary cancer. When compared to other cancer types, HCC is extremely complex and distinct. It is most commonly associated with chronic liver diseases like hepatitis or cirrhosis from any cause.[9]The Unani system of medicine is one of the oldest traditional medicinal systems, with centuries of experience treating chronic liver diseases and cirrhosis. A large number of single and compound drug formulations have been shown to improve chronic liver conditions.[10]There are a lot of medicinal plants that have anticancer properties. *Semecarpus anacardium* (Varnish tree) is one of them. It is a deciduous tree found in the sub-Himalayan and tropical regions of India.[11]This medicinal plant has long been used in Siddha and Ayurvedic medicine to treat a variety of ailments. *Semecarpus anacardium* Siddha preparation has already demonstrated anticancer efficacy against hepatocellular carcinoma.[12]

Liver diseases

The regulation of numerous physiological processes involves the liver in a significant way. It is involved in many essential processes, including metabolism, secretion, and storage. The liver can detoxify a variety of xenobiotics and medicines. The liver's bile acid, along with a few other factors, controls how food is digested. One of the most severe disorders is liver disease. It can be divided into three categories: cirrhosis (which leads to liver fibrosis), hepatizes, and chronic or acute (inflammatory sickness) (non-inflammatory ailment). They are mostly brought on by a number of risk factors that create oxidative stress in the liver, which in turn causes the peroxidation of lipids and other oxidative damages to the liver cells. Hepatitis and cirrhosis may occur from increased lipid peroxidation during the liver's microsomal ethanol metabolism.[13]

Risk factors for liver cancer

The common component causing liver cirrhosis is determined to be chronic infection with the Hepatitis C and B virus. [14]The use of contaminated needles and the sharing of blood are two ways that the hepatitis C and B viruses can spread from one person to another. Before blood transfusion, a blood test can help to limit this risk of transmission. [15]Alcohol abuse, which results in liver cirrhosis and hepatic cancer, is another risk factor.[16]Liver cancer risk can also be increased by smoking, being overweight, having diabetes, and using tobacco.[17]Additionally, prolonged exposure to thorium dioxide (an X-ray compound), vinyl chloride, and aflatoxin can increase a person's risk of developing cirrhosis and liver cancer.[18]

Pharmacological activity of Unani Herbs:

Baladur (Semecarpus anacardium L.)

Semecarpus anacardium L. is a dry deciduous important medicinal plant, belonging to the family Anacardiaceae. The word, Semecarpus is derived from Simeon in Greek means marking/tracing and carpus in Greek means nut. Anacardium means cardium, i.e., heart-shaped marking nut. It's an Indian species that can be found from the outer Himalayas to the Coromandel Coast. It's a close relative of the cashew.

(Fig. 1), (Fig. 2) and Table 1.

Fig.1. Flowering *Semecarpus anacardium* along with fruits/seeds.

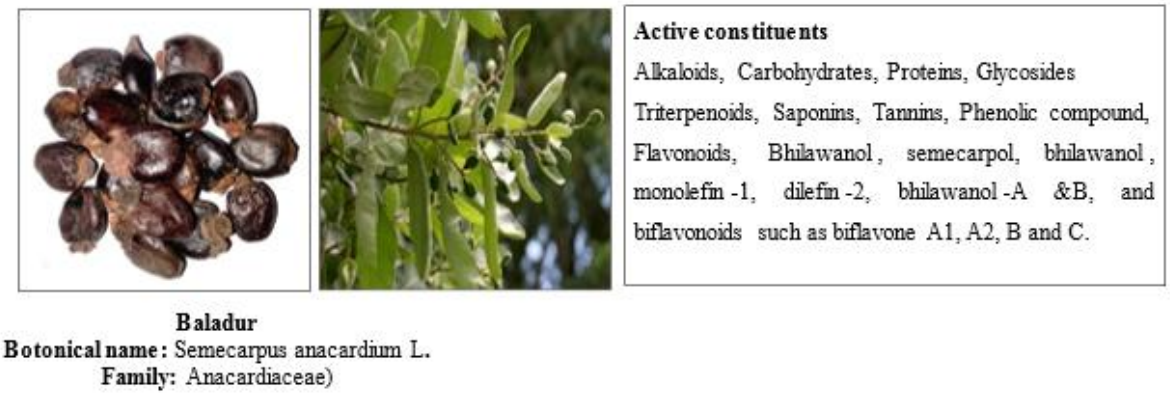

Fig. 2.Baladur and its active constituent.

Table-1 Summary of Unani drug

Name of Plant	Common Names	Short Details about plant	Active Constituents	Structure	Uses	Reference
Baladur (*Semecarpus anacardium L.)* (Family Anacardiaceae**)**	Bhela, Bhelatuki (Hindi and Beng); Balia (Oriya), and marking nut tree or Oriental cashew (English).	*Semecarpus anacardium* tree is found in abundance in Assam, Bihar, Bengal, Orissa, Chittagong and central India.	Alkaloids, Carbohydrates Proteins, Glycosides Triterpenoids, Saponins Tannins, Phenolic compound, Flavonoids, Bhilawanol, semecarpol, bhilawanol, monolefin-1, dilefin-2, bhilawanol-A &B, and biflavonoids such as biflavone A1, A2, B and C.	Biflavone	(Locally) wounds, migraine, uvulitis,boils, eczema, earache, hydrocele, localized pain, (Orally) bronchitis, asthma, helminthiasis, hemorrhoids, psoriasis, rheumatic complaints, neuralgias, tumors, etc. diabetes, geriatric problem, and various nervous etc.	[32]–[36]

Antioxidant Activity:

Very recently studied the antioxidant activity of aqueous and ethanolic extract of *Semecarpus anacardium* leaves. The antioxidant activity was measured using the DPPH method, and it revealed that the extracts possess significant antioxidant activity. The ethanolic extract possesses a scavenging activity of 36.70% whereas its aqueous extract had an activity of 22.21%. [19]

Examined antioxidant activity using DPPH free radical scavenging test. The IC_{50} values of SA extract and ascorbic acid in the DPPH scavenging assay were 72.24 g/ml and 17.81 g/ml, respectively. These findings suggest that stem barks of S. anacardium have high antioxidant activity and can be used as a natural antioxidant source in traditional medicine. [20]

Very recently studied to determine the antioxidant activity of acetone leaves extract of Semecarpus anacardium Linn. In this study, a Nitric oxide radical scavenging assay was used to study their inhibition percentage against the reactive oxygen species. The antioxidant activity of leaf extract of S. anacardium demonstrated an inhibition percentage of 42.28 ± 0.069 at 5 µg/ml and 53.03 ± 0.069 at 25 µg/ml respectively while that of the standard ABA showed 47.04 ± 0.069 at 5 µg/ml and 56.79 ± 0.069 at 25 µg/ml, both of these showing a significance values less than one. The in vitro antioxidant activity of acetone leaves extracts of Semecarpus anacardium revealed a significant antioxidant activity and its potential use in oxidative stress-related disease control.[21]

Anticancer Activity:

Very recently evaluated the effect of MESA (Methanolic leaves extract of Semecarpus anacardium) on NDEA (N-nitroso diethyl amine) induced hepatocellular carcinoma on Sprague Dawley rats. The hepatocarcinogen NDEA was administered at a dose of 200 mg/kg, single i.p., whereas MESA 200 mg/kg and 400 mg/kg were given daily orally for 12 weeks. The protective activity of MESA was measured using biochemical indicators such as SGOT, SGPT, ALP, and LDH. The livers were tested for alpha-fetoprotein and histopathological changes were examined. MESA restored antioxidant levels to near-normal levels and decreased the elevated serum levels of SGOT, SGPT, AST, LDH, and AFP. In mice treated with the extract, histopathological alterations such as necrosis, enlarged sinusoids, and increased inflammatory cell infiltrate were partially or completely prevented. According to the findings of this study, MESA was found to be high in antioxidants, and its active ingredients facilitated free radical scavenging activity. In the treatment of primary liver cancer, 400 mg/kg extract displayed a promising effect. [22]

Another study, determine the anticancerous efficacy of Semecarpus anacardium (SA) nuts. In this study, rats were divided into five groups. Group, I was assigned water control. The animals of groups II, III, and IV were used to induce hepatocellular carcinoma (HCC). N-nitrosodiethylamine was used as an inducing agent followed by phenobarbitone as a promoter for 13 weeks. Animals of Group-II were served as hepatocellular carcinoma control and kept untreated. Group-III animals were given an Ayurvedic milk extract of Semecarpus anacardium nuts at the dose recommended in Ashtangahridaya, an authentic Ayurvedic book for 49 days. group-IV animals were given doxorubicin at a dose of 1 mg/kg twice a week for seven weeks, as a reference medication. Group V animals were kept as drug control (SA nut milk extract) to assess the effect of nut milk extract on normal rats. After 154 days of in experiment, all of the animals were screened for HCC using liver enzymes, an HCC marker (alpha-2 macroglobulin), and histology. The hepatocellular carcinoma control group had higher liver enzymes and HCC marker, as well as neoplastic alterations in the liver, while the Semecarpus anacardium nut milk extract treated group had lower liver enzymes and HCC marker. The effect of doxorubicin and the Ayurvedic drug had a good association. The efficacy of Semecarpus anacardium nut milk extract for the treatment of hepatocellular carcinoma, either alone or in combination with chemotherapy, was proven in this study.[23]

Hepatoprotective activity:

Evaluated the hepatoprotective effect of fruit extracts of Semecarpus anacardium against the carbon tetrachloride (1.25mg/kg, p.o.) liver damage. Aqueous and ethanolic extracts of Semecarpus anacardium fruits were given orally for 7 days at doses of 250 and 500 mg/kg/day. The standard medicine was silymarin (50 mg/kg). To determine the hepatoprotective activity biochemical markers such as serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), alkaline phosphatase (ALP), total bilirubin, and serum protein were used. the result suggested Both aqueous and ethanolic extracts were found to have strong hepatoprotective efficacy However, the ethanolic extract has a higher hepatoprotective effect than the aqueous extract. [24]

Another studyreported that for hepatocellular carcinoma, nut extract was found to detoxify a potent hepatocarcinogen aflatoxin B_1 and cause its metabolites to be excreted in the urine, as well as having immune-modulatory, anti-oxidative, membrane stabilizing, tumor marker regulative, glucose level restoring, and mineral regulation properties.[25]

Antimicrobial Activity:

Investigated the Antimicrobial Activity of *Semecarpus anacardium* Nuts By using the Agar well method, the petroleum ether nut extract of Semecarpus anacardium showed antibacterial properties against both gram-positive and gram-negative bacteria. The inhibitory activity showed nut extract against test organisms like Micrococcus luteus (23 mm), Escherichia coli (19 mm), Bacillus subtilis (14 mm), Salmonella typhi (26mm), and Klebsiella pneumonia (22 mm). The antibacterial activity of Semecarpus anacardium nut extract is attributed to Petroleum Ether extractable components. The preliminary phytochemical analysis of Semecarpus anacardium revealed the presence of Triterpenoids, Anthraquinones, phenols, and steroids which have contributed to effective antibacterial activities. this study suggests that some of the plant extracts possess compounds with good antibacterial properties that can be used as antimicrobial agents in the search of new drugs. *Semecarpus anacardium* is strongly active against Salmonella typhi.[26].

Found the antimicrobial activity of *Semecarpus anacardium* (disc diffusion method) using various extracts. At a concentration of 100 mg/ml, the petroleum ether and aqueous extract fractions of *Semecarpus anacardium* displayed inhibitory efficacy against Staphylococcus aureus (10 mm) and Shigella flexneri (16 mm). While Bacillus licheniformis, Vibrio cholera, and Pseudomonas aeruginosa were inhibited by chloroform extract, Pseudomonas aeruginosa and S. aureus were inhibited by ethanol extract.[27]

Reported that an alcoholic extract of *Semecarpus anacardium* dry nuts was revealed. In vitro bactericidal activity against three gram-negative pathogens (Escherichia coli, Salmonella typhi, and Proteus Vulgaris) as well as two gram-positive strains (Staphylococcus aureus and Corynebacterium diphtheriae) Following tests, it was shown that the alcoholic extracts of several sections of the plant (leaves, twigs, and green fruit), particularly the leaf extract, exhibit antibacterial characteristics.[28]

Antidiabetic Activity:

Investigated *Semecarpus anacardium's* antidiabetic activity (Linn.). Alloxan-induced diabetic rats were used to determine the antidiabetic activity. Serum biochemical markers such as TC, TG, LDL, HDL, SGOT, and SGPT were measured after 15 days of treatment. The survival rate, body weight, organ weight, liver glycogen, and haematological parameters (RBC and Hb) were also measured. The rats in Group SA 400 had a 100% survival rate, according to the findings. Throughout the treatment period, the effect of the extract on blood glucose levels in Groups SA 100, SA 200, and SA 400 was dose-dependent. No significant changes were observed in organ weight to body weight ratio, however, liver weights improved significantly in Groups SA 200 and SA 400. The bark extract showed significant (p 0.05) anti-diabetic efficacy, decreasing TC, TG, and LDL levels in a dose-dependent manner while also protecting the liver, which could be explained in part by lower SGOT and SGPT levels as well as increased liver glycogen. The Hb and RBC count percentages were negatively correlated with the doses of extracts. These findings suggest that the stem barks of S. Anacardium have potent anti-diabetic properties, implying that they can be used to treat diabetes mellitus in traditional medicine.[20]

Another study investigated the Semecarpus anacardium's anti-diabetic potential in Type 2 diabetic rats caused by a high-fat diet (HFD) for 2 weeks followed by a single intraperitoneal injection of streptozotocin (STZ) 35 mg/kg body mass. After 3 days of STZ induction, the hyperglycaemic rats were given Semecarpus anacardium nut milk extract (SA) orally at a dose of 200 mg/kg body weight daily for 30 days. The standard medicine was metformin (500 mg/kg body weight, orally). The values of fasting blood glucose, insulin, Hb, HbA1c, HOMA-IR, and HOMA-β were all tested. When compared to the HFD STZ control group, SA considerably ($p<.05$) reduced and normalized blood glucose levels, as well as decreased HbA1c levels. The presence of flavonoids in the medication could explain its antihyperglycemic and antioxidant properties.[29]

Anti-arthritic Activity:

Investigated that the effect of *Semecarpus anacardium Linn.* nut milk extract (SA) on the metabolism of bone turnover has been studied by analysing various markers of bone turnover and by histological and radiological analysis of the joints in adjuvant arthritis in rats. In rats, arthritis was generated by injecting Freund's complete adjuvant comprising 10 mg of heat-killed Mycobacterium tuberculosis in 1 ml paraffin oil (0.1 ml) intradermally into the rat's left hind paw. was able to significantly reverse the changes in bone turnover seen in arthritic animals by regulating calcium, phosphorus, and the activity of the enzyme's tartrate-resistant acid phosphatase, acid phosphatase, and alkaline phosphatase. The medicine restored bone weights that had been lost due to arthritis. Protective activity of SA was also observed by the decrease in the levels and expression of tumor necrosis factor-alpha (TNF-a) as well as the histopathological and radiological observations. All of these findings suggest that SA has potent anti-arthritic properties by modulating bone turnover.[30]

Another study, reported inflammation amplifies the effects of NO radicals, which are fat-soluble. Because of its antioxidant properties, SA induces a considerable drop in nitrate/nitrite levels.[31]

CONCLUSION

Our knowledge of herbal active ingredients and herbal composite formulas for the control and diagnosis of Hepatocellular carcinoma will be improved as a result. It is possible to create novel therapeutics thanks to the discovery that *Semecarpus anacardium* is a source of medicinally usable products with a broad range of pharmacological activities. It's a common practice in the traditional healthcare system. In addition to other diseases, they offer important protection against a variety of malignancies. There is now no known cure for cancer, even though several scientific studies have been conducted to investigate the anticancer and other properties of this natural substance. *Semecarpus anacardium* anti-cancer plants have been explored in this review. These herbs have anticancer potential due to their hepatocellular carcinoma and antioxidant capabilities. Knowledge on anticancer medicinal plants used by people from around the world from different countries is also included in this article. Utilizing cutting-edge anticancer medications made from therapeutic plants is also essential.

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Conflict of Interest:
The authors declare that they have no conflict of interest.

Ethical approval:
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