Review Article

Phytochemical, Biological and Traditional Claims on *Averrhoa bilimbi*: An Overview

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Garg *et al.*: Recent updates on *Averrhoa bilimbi*: An approach

***Averrhoa bilimbi* is primarily utilized in traditional medicine to cure blood pressure, high levels of sugar in the blood and many infectious diseases. The key objective of the current review is to assemble and establish literature based on traditional claims and relate those with up-to-date pharmacological results on the use of *Averrhoa bilimbi* for managing diverse diseases. Literature was collected, systematically assessed, understood and discoursed from the various scientific databases as Scopus, PubMed and ScienceDirect by using keyword *Averrhoa bilimbi*. Various biological activities have confirmed the potential of *Averrhoa bilimbi* to act as antioxidant, antimicrobial, antidiabetic, hypotensive, anti-inflammatory and hepatoprotective which indicates the excessive worth of plant holds as complementary and alternative medicine. Consequently, it is aimed to compile a current and complete review of *Averrhoa bilimbi* which offsets its traditional uses as medicine, phytochemistry and biological effects.**

Key words: *Averrhoa bilimbi*, phytochemistry, nano-formulations, pickle tree, Oxalidaceae

Averrhoa bilimbi (*A. bilimbi*) is a long-lasting green plant of the Oxalidaceae family, having 16-33 ft. in height, with a short trunk, which is divided into several branches and it contained many eatable fruits. The name of the plant was derived from an Arab Philosopher and physician, commonly known as Averroes. *A. bilimbi* firmly resembled *Averrhoa carambola* (star fruit) [1]. Popularly, this is found in tropical and subtropical regions like Malaysia, Myanmar, Indonesia, Thailand, Singapore, Philippines, Srilanka, India, Bangladesh, etc. In India, Kerala is well known for its appropriate abundance, predominantly, used by the Kani tribal traditional healers in the Tholu hill region. The local name of this plant in Kerala is Irumban puli or Pulingi. Leaves and fruits have been used for circulatory system diseases for decades[2,3]. Commonly, the plant is also known as cucumber tree, tree sorrel, *bilimbi*, pickle tree (English), pias and kamias (Philippines), Huang gua shu (Chinese), Ta ling pling (Thai), *bilimbi* and Irumban puli (India), Bilimbim, biri-biri and Azedinha (Brazil), Khe Tay (Veitnamese), belimbing buluh and blimbing asam (Malaysia) and Taling Pling (Thailand) [4]. In Indonesia, belimbing wuluh (*A. bilimbi* Linn) is popular for its sour taste and characteristic essence and is used as a flavouring agent for cooking purposes[5].

Literature survey revealed the use of the plant in folk medicine as antidiabetic, antimicrobial, and antihypertensive[3]. Different parts of plants like leaves, seeds, bark, fruits, flowers and roots as well as the entire plant as a whole have been used as an alternative for the treatment of many diseases, mainly utilized as antidiabetic agents[6]. Usually, it is employed to treat cold, cough, skin rashes, swellings in joints, whooping cough and high blood pressure. The plant showed antibacterial activities against both positive and negative gram stains[7] and showed cytotoxic[8], antifungal[9], anti-hyperglycaemic activities too as it abolished the serum insulin level in diabetes mellitus[10]. The presence of plentiful phytoconstituents like alkaloids, glycosides, tannins, steroids and saponins, in different parts of the plant, reflected its potential in the treatment of several diseases[11]. Free radical scavenging properties displayed by fruit extract confirmed its role in the treatment of cardiovascular diseases, inflammatory conditions, aging, as a facial moisturizer and in the management of cancer[2,12]. The key emphasis of this article is to provide the useful side including its botanical aspects, ethnopharmacology and

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phytochemistry as well as to introduce the outstanding therapeutic potential of the plant.

BOTANICAL ASPECTS

A. bilimbi is a small tree of 15 m height having sparingly organized branches and bears compound hairy leaves (5-10 cm long) of pinnate shape comprising of twenty to forty leaflets each forming cluster at the end of branches[13]. The tree is cauliflorous including 18-68 flowers in panicles, which form the branches and the trunk. Flowers are hetero-tristylous, yellowish-green to reddish-purple in colour having 10-30 m long petals as shown in fig. 1[4]. They are grown on the bare trunk and stem, greenish in colour with juicy and firm flesh at the beginning that turned to soft upon ripening[13]. The fruit juice is sour in taste and enormously acidic. The outer skin of the fruit is very thin, glossy, soft and tender. The tree is often cultivated for its fruits in many areas.

GEOGRAPHIC DISTRIBUTION

Native:

Indonesian Moluccas and West Malaysia.

Exotic:

Argentina, Australia, Brazil, Philippines, Puerto Rico, Singapore, Colombia, Cuba, Ecuador, Guyana, Trinidad and Tobago, United States of America India, Jamaica, Myanmar, Sri Lanka, Bangladesh, Surinam, Tanzania, Thailand, Venezuela[9,11]. Fig. 2 depicted the geographical distribution of *A. bilimbi*.

Fig. 1: Representing *A. bilimbi* tree, flowers, leaf and fruits

Fig. 2: Map showing the geographical distribution of the plant
Note: ( ): Native range and ( ): Exotic range

ETHNOPHARMACOLOGY

Traditionally, it has been used for the treatment of diverse illnesses in different parts of countries[14]. Paste of leaves used for treating boils, itches, skin irruptions, rheumatism, cough, mumps, colds, syphilis and bites of toxic creature[15]. Likewise, decoction and infusion of the leaves has been used as an antiscorbutic, protein precipitation, antibacterial, in pyresis, in rectum inflammation, in diabetes control and as postpartum protective medicine[14]. Apart from this fruit juice is used for treating bilious colic, scurvy, whooping cough, obesity, diabetes and hypertension[16] while, grated fruits with a little salt are applied on the skin to cure pimples[17].

EXTRACTION METHODS

Recently bioactive constituents isolated from the plant become a point of attention in the pharmaceutical and food market, leading to development of amazing technologies for extracting important phytoconstituent from the plant. Numerous methods have been listed in the literature regarding extraction of phytoconstituents from the *A. bilimbi* namely ultrasound-assisted extraction and maceration[18].

Ultrasound-assisted extraction:

This method was performed in a 50 ml centrifuge tube using the ratio of plant to solvent as 1 g in 20 ml. The tube was subjected to 25 kHz ultrasonic radiations in the ultrasonic bath followed by the addition of water to fill three-quarters of the tube and kept under the same condition throughout the process to confirm the transmission of the ultrasound waves from the transducer to the sample. The required time for extraction was set to 60 min while the temperature of the water bath was kept at 30°. The extraction was performed with different solvents like 80 % ethanol, 20 % distilled water and distilled water using the same method[19].

Maceration:

The samples were extracted *via* maceration with different solvents like 80 % of ethanol, 20 % distilled water; 80 % of methanol, 20 % distilled water and distilled water. For each mixture plant-solvent ratio was kept to 1 g:20 ml. The extraction involved continuous stirring of plant material in related solvent at 300 rpm for 48 h afterwards sample was filtered and dried using rotary vacuum evaporator at 50° temperature[20].

PHYTOCHEMISTRY

As per the literature survey, various phytoconstituents were extracted from the plant such as alkaloids, saponins, phenols, carbohydrates, tannins and flavonoids, and their presence was confirmed through preliminary phytochemical screening procedures. Different parts of plants were found to possess varied compounds in different concentrations[2].

Preliminary phytochemical screening results showed the presence of alkaloids, saponins, flavonoids, cardiac glycosides, triterpenes, carbohydrates and tannins have been confirmed[21]. Furthermore some new compounds namely 2,3-bis(2,6,10-trimethylundeca-1,5,9-trienyl) oxirane, squalene, 3-(6,10,14-trimethylpentadecan-2-yl) furan-2 (5H)-one, phytol, 3,4-dihydroxyhexanedioic acid were isolated from the methanolic extract of the leaves[22].

Auw *et al.* isolated 3 new compounds along with 12 known compounds namely Beta (β)-amyrenone, β-amyrin,phytol,β-sitosterol,stigmastanol,aurantiamide benzoate, trans-cinnamic acid, 4-hydroxycinnamic acid, phloretic acid, (S)-dehydrovomifoliol, (6S,7aR)-loliolide and carambolaflavone from ethyl acetate extract of leaves as shown in fig. 3[23].

From preliminary phytochemical screening and chromatograms presence of carbohydrates, flavonoids, polypeptides, bitter principles, amino acids, oxalic acid, polyphenols, volatile oil, coumarin, valepotriates and terpenes in the fruit was confirmed. Investigation was completed by the appearance of vitamin C and oxalic acid in the fruit extracts[24,25].

Data obtained from previous research findings showed the presence of 53 volatile constituents in the Malaysian *bilimbi* fruit. Aliphatic acids contributed about 47.8 % of the total volatiles with key constituents like 2-furaldehyde (19.1 %), hexadecenoic acid (palmitic acid) (10.2 %) and (Z)-9-octadecenoic acid (10.2 %). 12 compounds were traced as esters compounds and found to be present in the fruit and among them hexyl nicotinate (1.7 %) and butyl nicotinate (1.6 %) were reported in higher concentrations[26].

In another study the plant grown in Cuba when subjected to isolation procedures yielded about 6 mg/kg of total volatiles from the pulp of the fruit and approximately 62 new compounds were isolated from it. The compounds were named as nonanal (2.7 mg/kg),

nonanoic acid (0.25 mg/kg), (Z)-3-hexenol (0.48 mg/kg), tricosane (0.27 mg/kg), hexadecenoic acid (0.31 mg/kg), (E)-2-decenal(0.26 mg/kg), (Z)-9-pentacosene (0.24 mg/kg), (Z)-9-tricosene and 2-furfural (0.18 mg/kg) were identified as main constituents in the pulp of the fruit. The compounds like nonanal, (E)-2-nonenal, (Z)-3-hexanol and nonanoic acid were found to be responsible for the fatty and green appreance of the fruit[27].

PHARMACOLOGICAL POTENTIAL

Pharmacological investigations carried out on the different parts of the plant revealed its therapeutically efficacy as antidiabetic, antimicrobials, cytotoxic, hepatoprotective, wound healing, anthelminthic, antioxidant, hypolipidemic, antithrombotic and antihypertensive as shown in fig. 4.

Antioxidant:

Antioxidants are compounds that neutralize free radicals and prevented cellular damage. They also exhibited an important role in the diseases related to oxidative stress like cancer, neurodegenerative disorders and diabetes mellitus[28]. The ethanol extract of the leaves exhibited a significant photo protective effect against the ultraviolet light-induced oxidative damage in the albino mice and the same was further potentiated by diminished photo-aging induced by UV-light on the skin of mice induced after topical application (4 %) of leaves extract and it could be attributed due to reduced malondialdehyde level up to 50 % as compared to control group. It was further observed that the animals treated with the same extract exhibited lesser incidences of dermatitis and histological changes in reference to untreated ones that in turn reflected their anti-aging properties[29].

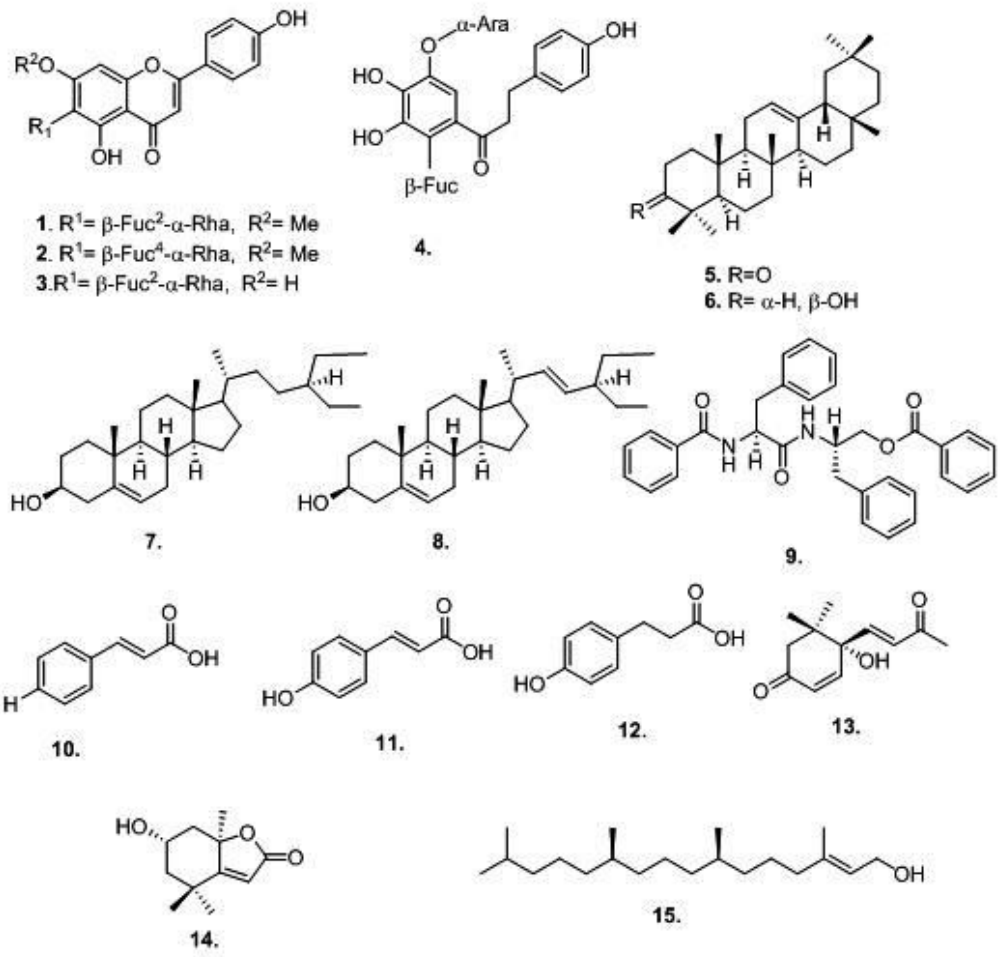

Fig. 3: Phytoconstituents isolated from the leaves extract

Note: (1,2,3): New compounds; (4): 1-(3,4-dihydroxy-5-methoxy-2-methylphenyl)-3-{4-hydroxyphenyl)propan-1-one 3=carambolaflavone; (5): R=O; (6): R= α-H, P-OH; (7): b-sitosterol; (8): Stigmastanol; (9): Aurantiamide benzoate; (10): Trans-cinnamic acid; (11): 4-hydroxycinnamic acid; (12): Phloretic acid; (13): (S)-dehydrovomifoliol; (14): (6S,7aR)-loliolide,(6S,7aR)-6-hydroxy-4,4,7a-trimethyl-5,6,7,7a-tetrahydrobenzofuran-2(4H)-one) and (15): Phytol

Fig. 4: Pictorial depiction of therapeutic indications of the *A. bilimbi*

One of the studies demonstrated the antioxidant potential of the *A. bilimbi* in the lipopolysaccharides induced production of macrophages and results obtained verified significant antioxidant activity exhibited by the extract at 0.02 % w/v concentration in thiobarbituric acid and ferric thiocyanate based assay procedures whereas in 2,2-Diphenyl-1-(2,4,6-Trinitrophenyl)Hydrazyl (DPPH) assay, leaves extract were proven to be inactive while fruit extract was recognized as strong antioxidants with half-maximal Inhibitory Concentration (IC_{50}) value of 20.35 µg/ml and reported with the outstanding antioxidant ability (417.093±6.577) mg/g in terms of the AAE[28] supported by other studies too[30].

Literature studies confirmed the free radical scavenging as well as xanthine oxidase inhibitory properties of methanolic extract of the leaves through DPPH assay with IC_{50} (4.14±0.21) µg/ml ($p<0.05$) and IC_{50} (64.84±3.93) µg/ml ($p<0.05$) respectively[31]. Similarly, another study conducted on the different extracts of the fruits revealed the excellent DPPH free radical scavenging activities exhibited by the crude methanolic extract (IC_{50}=30.365 µg/ml) followed by chloroform (IC_{50}=32.852 µg/ml), Carbon Tetrachloride (CCl_4) extract (IC_{50}=36.708 µg/ml), pet ether (IC_{50}=50.35 µg/ml) and aqueous soluble fraction (IC_{50}=79.918 µg/ml)[24]. One study stated the significant free radical scavenging activities and remarkable total antioxidant capacity with IC_{50}=20.35 µg/ml and (417.093±6.577 mg/g in Ascorbic Acid Equivalent (AAE)) respectively[11].

Antimicrobial:

A literature survey on the antimicrobial potency of different parts of the *A. bilimbi* has been reported. The ethanol extract of the leaves exhibited significant antimicrobial potency against six pathogenic microorganisms including two gram-negative (*Escherichia coli* and *Pseudomonas aeruginosa*), two gram-positive bacterias (*Bacillus megaterium* and *Bacillus cereus*) and two fungi (*Cryptococcus neoformans* and *Aspergillus ochraceous*)[32]. Chloroform and aqueous extract of the fruit and leaves (100 mg/ml) of plant has been reported to possess antibacterial activity against *Staphylococcus epidermidis, Staphylococcus aureus, Bacillus cereus, Citrobacter freundii, Salmonella typhi,*

Proteus vulgaris, Kocuria rhizophila and *Aeromonas hydrophila*[33]. Antibacterial action was displayed by the whole *bilimbi* fruit and fruit juice (not filtered) against *Salmonella typhimurium* and *Listeria monocytogenes* Scott A. One of the studies revealed the use of *A. bilimbi* as a natural method of decontamination in fruits preparations as it was observed to reduce microbial load of *Listeria monocytogenes* Scott A and *Salmonella typhimurium* in raw shrimps[34] added by another one where the antimicrobial efficacy of the root and fruit extract against *Mycobacterium tuberculosis* was confirmed at Minimum Inhibitory Concentration (MIC) value of 1600 µg/ml[35] in synergy with antifungal effect against *Candida albicans, Blastomyces dermatitidis, Cryptococcus neoformans, Trichophyton species and Pityrosporum ovale* at MIC values ranging from 15.65-62.50 µg/ml[9].

Antidiabetic:

Significant sugar lowering effect of extracts of the leaves prepared in ethyl acetate, hexane, aqueous fraction and butanol was reported at 125 mg/kg *A. bilimbi*, for evaluating hypoglycaemic effect in Streptozotocin (STZ) diabetic male Sprague-Dawley rats. Results obtained revealed the significant effect of the aqueous fraction of the plant *via* enhancing glucose tolerance and improving insulin secretion, which overall resulted in increased serum insulin level, assumed as a possible mechanism for the hypoglycaemic activities[36]. Other investigations performed on a high-fat diet-fed STZ-induced model using the same extracts reported the significant activities of the butanol and aqueous fraction[37]. Likewise, hypolipidemic and hypoglycaemic properties of the ethanol extract of the leaves at 125 mg/kg were found to cause lowering of triglycerides and glucose levels in rats having STZ-induced diabetes[38].

Outcomes of *in vitro* studies revealed the strong Alpha (α)-glucosidase inhibitory activities by the ethanol extract of the plant and it was found to be inactive against α-amylase[39] and the same was confirmed by the strong inhibition of protein tyrosine phosphatase by the leaves extract[40]. Investigations on the effects of ethyl acetate fraction of the fruit in dose of 25 mg/kg for 2 mo resulted in a significant decline in the glycated haemoglobin, serum glucose level and notable reduction in thiobarbituric acid-reactive substance, hydroperoxide and conjugated dienes along with an increase in plasma insulin level added by, a significant increase in the catalase, Glutathione (GSH) reductase, GSH peroxidase and Superoxide Dismutase (SOD), that in turn affected in the modulation of hepatic antioxidant potential. Histopathological annotations confirmed the successful rescue of the hepatocytes from oxidative damage by the plant extract. The overall results obtained were quite comparable to the standard drug metformin[41].

Protective in ulcerative colitis:

The disease is characterized by a persistent form of inflammation, mainly affecting colon mucosa and tissues. Fruit extract of a plant at 50 mg/kg body weight and 100 mg/kg body weight showed a significant effect in acetic acid-induced ulcerations in the Wistar rat when given for 6 d through the intraperitoneal route. The main parameters altered in the process decreased in the mucosal injury, reduction in Interleukin-(IL)-1β, IL-6 and Tumor Necrosis Factor-Alpha (TNF-α) level, increased tissue weight of colon and spleen and reduction in inflammatory markers i.e. Cyclooxygenase-2 (COX-2) and inducible Nitric Oxide Synthase (iNOS), the observed responses were modulated by antioxidant activities, exerted *via* diminishing NO level and improving SOD and GSH in the respective organs[42].

Anti-hypertensive:

Usually, the leaves and fruits of the *A. bilimbi* have been used effectively used for symptomatic relief in the treatment of hypertension. A significant reduction in the contractility of the nor epinephrine-induced guinea pig atria was reported without disturbing beating regularity by the aqueous extract of the plant in an *in vitro* isolated organ model[43]. Similarly, antihypertensive activities of the leaves extract in an *in vivo* protocol were confirmed when performed on the cats[44].

Anti-inflammatory agent:

Significant inhibition in inflammation was caused by the methanolic extract of the leaves in the enema of the paw caused by an irritant i.e., carrageenan. Responses obtained were comparable to ibuprofen and sustained for the 2-4 h whereas analgesic effect (67.51 %) was noted at 400 mg/kg against acetic acid-induced pain and found to be comparable to diclofenac sodium that exhibited 64.33 % analgesic effect at 10 mg/kg dose[45].

Hepatoprotective:

The methanolic extract of the leaves was effective against CCl_4 induced hepatotoxicity in Wistar rats at 250 and 500 mg/kg. The main outcomes included reduced levels of liver biomarkers i.e., Serum Glutamate Pyruvate

Transaminase (SGPT), Serum Glutamate Oxaloacetate Transaminase (SGOT), bilirubin and total proteins in rats[46]. Studies performed in albino rats too resulted in almost similar outcomes[47]. The fruit extract has also been reported to be efficacious against acetaminophen-induced hepatic damage in the Wistar rats at similar doses as for the above-mentioned groups[48].

Antibacterial:

The recent studies demonstrated the significant antibacterial effect of the fruit extract against multidrug-resistant bacteria based on findings obtained from the zone inhibition method and calculated the bactericidal concentration (MBC) using Mueller Hinton broth in a micro-dilution method. The ethanol extract of the plant exhibited significant antibacterial activities (10-14.5 mm) in the proposed assay and also affected the bacterial inhibition of aqueous ones against Extended Spectrum β-lactamase+Carbapenemase (ESβL+CR) *Pseudomonas aeruginosa* (12.5 mg/ml)[49].

Anticancer agent:

Some authors also reported the cytotoxic potential associated with the ethanol leaves to extract the plant at Lethal Concentration 50 (LC_{50}), 5.81 µg/l in brine shrimp lethality assay[7] supported by the significant activity of methanolic extract of fruits and its CCl_4 and petroleum ether fractions at LC_{50} of 0.005 µg/ml, 1.198 µg/ml and 0.781 µg/ml, respectively in reference to vincristine sulphate at LC_{50} of 0.839 µg/ml. Chloroform and aqueous soluble portions also demonstrated the cytotoxic behaviour corresponding to the values equal to LC_{50} of 5.691 and 6.123 µg/ml, respectively[50]. Findings on plants suggested the potential of the ethanol leaves and methanolic fruit extracts in the management of MCF-7 breast cancer cell lines corresponding to IC_{50} of 668 µg/ml and 154.9 µg/ml respectively[51]. Efficacy of fruit extract in Dalton's Ascetic Lymphoma (DAL) too was confirmed through the 3-(4,5-dimethylthiazol-2yl)-2,5-diphenyltetrazolium bromide (MTT) assay wherein treatment with the extract resulted in lowering of an elevated number of white blood cells and raised the red blood cells and haemoglobin count, as compared to the control group. Also, a significant reduction in body weight was observed in the treated group with a growth inhibition rate (97.96 %) in the MTT assay[52]. Previously reported studies confirmed the anti-proliferative effect of the ethanol extract of the plant against hormone-dependent breast cancer cell lines (MDA-MB-231) by affecting the inhibition of the MDA-MB-231 cells *via* induction of apoptosis at Gap/Growth 1 (G_0/G_1) phase of cell cycle and of p53-independent mitochondrial apoptotic pathways[53].

Wound healing agent:

A. bilimbi is popularly known for its use in oral injuries as ethanol extract of leaves in the gingival wound healing have been reported. The study demonstrated that the application of 10 % leaves extract enhanced the gingival wound healing and increased the number of fibroblasts in the male rat in comparison to the control group[54].

Miscellaneous applications:

Literature survey on the plant clearly showed its outstanding worth in the treatment of diseases including the anticoagulant effect of ethanol extracts at 250 mg/kg in the normal and alloxan treated diabetic rat by prolonging prothrombin time and improved the thrombolytic potential of the methanolic extract[55,56]. In connection with findings pointing towards the hypolipidemic activities of the ethanol extract results obtained stated a significant lowering in the blood triglycerides level, enhanced antiatherogenic index, improved High-Density Lipoprotein (HDL) cholesterol to total cholesterol ratio at 250 mg/kg/d dose of the ethanol leaves extract when compared to the vehicle in the STZ-induced diabetic rats[38]. In another study leaves, the extract was also reported to inhibit cholesterol uptake in an *in vitro* assay in the human colon adenocarcinoma Caco-2 cells. In the model of intestinal absorption the lipid-lowering potency of fruit (125 mg/kg) and its aqueous extract (50 mg/kg) in the high-fat diet-fed rat were also found to be significant[57]. Some studies also reported the antifertility effect of the butanol fraction of the ethanol extract and that could be attributed due to the presence of steroidal glycosides and potassium oxalate constituents of leaves extract[58]. The therapeutic efficacy of different plant parts and extracts *A.bilimbi* depicted by various mechanisms has been listed in Table 1.

TOXICITY ASSOCIATED WITH PLANT

The fruit of *A. bilimbi* is comprised of the huge amount of oxalic acid. Extreme ingestion of fruit juice resulted in the accumulation of crystals of calcium oxalate in renal tubules, which leads to acute kidney failure. Some authors reported data collected from the five hospitals in the Kerala state of India, representing an acute renal failure after intake of fruit juice (100-400 ml/d). Entire patients had severe renal failure, having serum creatinine levels 5.5-12.3 mg/dl and acute tubular necrosis with

calcium oxalate crystals observed *via* kidney biopsy. Out of 10 patients, 7 needed haemodialysis, but luckily all improved to normal condition after 2-6 w of treatments[59]. Other researchers also reported two cases of acute nephropathy with oxalate crystals deposition in the renal tubules after consuming fruit juice[60].

NANO-FORMULATIONS

Currently, nanotechnologies are the most active disciplines of research in the modern science where plants and its phytoconstituents found an imperious use in the nana-particles synthesis as shown in fig. 5[61].

TABLE 1: THERAPEUTIC EFFICACY OF DIFFERENT PLANT PARTS AND EXTRACTS *A. bilimbi* DEPICTED BY VARIOUS MECHANISMS

Plant part extract	Animal model/Assay	Mechanism	Therapeutic role	References
Leaves ethanolic extract	Albino mice model	Reduced malonaldehyde level	Photo protective	[29]
Leaves methanolic extract	DPPH assay	Free radical scavengers	Antioxidant	[28]
Leaves ethyl acetate, hexane, butanol extract	Male Sprague Dawley rat model	Enhance glucose tolerance and improve insulin secretion	Hypoglycaemic	[36]
Leaves ethanolic extract	STZ-induced diabetic rat model	Lower triglycerides level and blood glucose level	Hypolipidemic and hypoglycaemic	[38]
Fruit extract	Acetic acid treated Wistar rat	Reduce IL-1b. IL-6, TNF-α level	Anti-ulcerative colitis activities	[42]
Leaves and fruits aqueous extract	*In vitro* isolated organ model	Reduction in contractility of nor epinephrine induced guinea pig atria	Antihypertensive	[43]
Leaves methanolic extract	Acetic acid induced pain in mice	Altered inflammatory mediators	Anti-inflammatory	[45]
Leaves methanolic extract	CCl_4 induced hepatotoxicity in Wistar rats	Modification in liver biomarker like SGPT, ALT etc.	Hepatoprotective	[46]
Fruits methanolic extract	MTT assay/DAL in mice model	Decrease WBC count and increase RBC and haemoglobin level	Anticancer	[52]

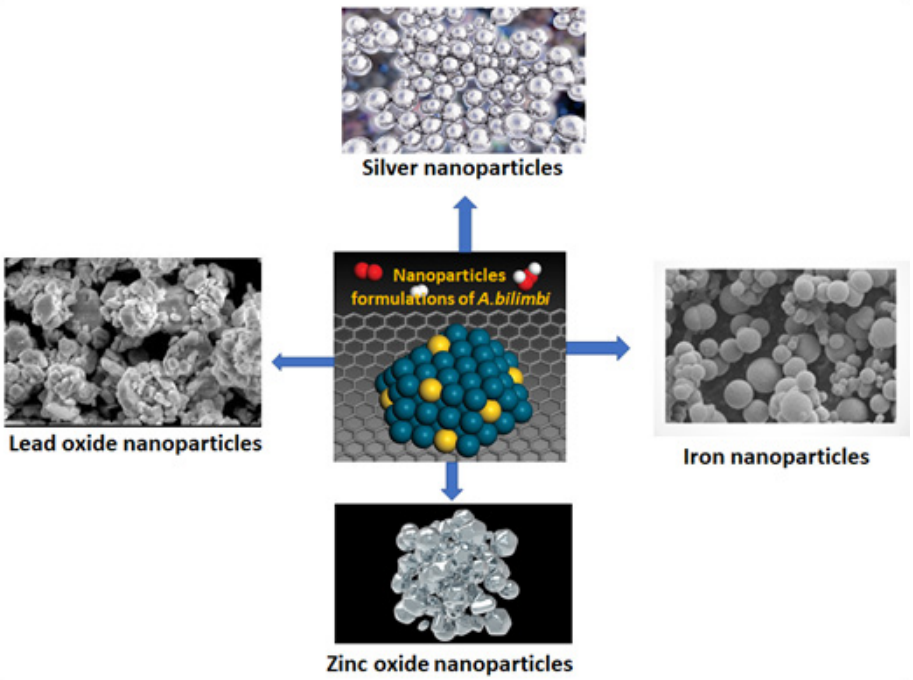

Fig. 5: Nano-formulations reported so far of the *A. bilimbi*

Silver nanoparticles:

The silver nanoparticles of leaf extract have been prepared by adding 5 ml of leaf extract drop wise into the 95 ml aqueous solution of Silver Nitrate ($AgNO_3$) with stirring at 50°-60° continuously and formation of nanoparticles has been confirmed through change in colour from white to reddish brown due to surface plasmon resonance. The prepared nanoparticles exhibited potent antibacterial activities against *Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa* and *Klebsiella pneumoniae* confirmed through agar well diffusion method and MIC method[62]. Another study also reported the one-way green synthesis of silver and gold nanoparticles of the *A. bilimbi* fruit extract[63].

Iron nanoparticles:

The iron nanoparticles have been prepared using Iron (III) Chloride Hexahydrate ($FeCl_3.6H_2O$), Iron (II) Sulphate Heptahydrate ($FeSO_4.7H_2O$) and plant extract. $FeCl_3.6H_2O$ and $FeSO_4.7H_2O$ were prepared and mixed in a beaker in the ratio of 2:1 using magnetic stirrer and then 5 ml plant extract was added and mixed for 1 h and nano-particle formation was confirmed by the change in colour to dark green or black. The prepared nanoparticles showed potent antioxidant properties confirmed through DPPH assay[64].

Zinc oxide nanoparticles:

Recently, Zinc Oxide (ZnO) nanoparticles of the fruit extract of *A. bilimbi* were prepared with the co-precipitation method, using zinc acetate dihydrate as a precursor. In this preparation, fruit extract was used as a capping and reducing agent. The formation of nanoparticles was confirmed with the help of UV-spectroscopy and X-ray diffraction techniques while size and shape were confirmed with electron microscopy[65].

Lead oxide nanoparticles:

The lead oxide nanoparticles of the fruit aqueous extract have been prepared by adding lead nitrate to it at room temperature in the dark and incubated for 24 h. The biological method has been used for the synthesis purpose as chemical methods led to the production of toxic compounds. The formation of nanoparticles has been confirmed by Scanning Electron Microscopy (SEM), X-ray spectroscopy, Fourier Transform Infrared Spectroscopy (FTIR), etc. These are eco-friendly, low-cost and non-pollutant[66].

CONCLUSION

Many research articles evolved on *A. bilimbi* showed that it contains enormous pharmacological properties. A variety of phytoconstituents present in it showed several medicinal actions. Many other types of research on biological evaluation and isolation of phytoconstituents from *A. bilimbi* need to explore that may be useful for improving human health in the coming days.

Conflict of interests:

The authors declared no conflicts of interest.

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