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Review on Terminalia Bellirica

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Abstract
Herbal medicines continue to play a vital role in primary healthcare systems, particularly in developing countries where traditional remedies remain widely practiced. The increasing global interest in herbal therapeutics is largely attributed to their safety, efficacy, and broad therapeutic potential compared to synthetic pharmaceuticals. Among medicinal plants, the genus Terminalia (family Combretaceae) is of significant pharmacological importance, comprising nearly 250 species distributed across tropical and subtropical regions of Asia, Africa, Australia, and Madagascar. Terminalia bellerica Roxb., commonly known as Bibhitaki or Baheda, is a prominent medicinal plant extensively used in Indian, Tibetan, and Chinese traditional medicine systems. It is one of the three constituents of the classical Ayurvedic formulation Triphala and is traditionally employed for the treatment of gastrointestinal disorders, liver diseases, respiratory ailments, inflammation, and metabolic disturbances.
Morphologically, T. bellerica is a large deciduous tree characterized by a straight trunk, spirally arranged leathery leaves, small yellowish-white bisexual flowers, and drupe-type fruits with a single hard seed. Phytochemical investigations of the fruits have revealed the presence of bioactive compounds such as gallic acid, ellagic acid, chebulagic acid, ethyl gallate, tannins, lignans, flavonoids, β-sitosterol, and various carbohydrates, with gallic acid being the major polyphenolic constituent.
Pharmacological studies have demonstrated that T. bellerica exhibits a wide range of biological activities, including antidiarrheal, analgesic, antihypertensive, antimicrobial, antioxidant, hepatoprotective, immunomodulatory, wound healing, antipyretic, anticancer, antithrombotic, antiulcer, antibiofilm, and β-lactamase inhibitory effects. Toxicological evaluations indicate that the plant is relatively safe at therapeutic doses. Overall, Terminalia bellerica represents a valuable source of bioactive compounds with significant therapeutic potential, supporting its traditional use and highlighting its promise for future drug development.

Keywords: *Terminalia bellerica, Chemical Compounds, Plants Bioactivites, Therapeutic Potential, Pharmacological Uses.*

INTRODUCTION:

Herbal medicines are used as a health care tool in different countries. All the developingcountries are fully dependant on herbal remedies. The use of herbal medicine is increasingdue to its safety, efficacy and therapeutic potential as compared to synthetic pharmaceutical products. However, the potential of higher plants as a source of herbal medicine isunexplored. Terminalia, comprising about 250 species in the world mostly as medium or large trees, is the second largest genus in the family Combretaceae. The name “Terminalia”is derived from Latin word “terminus”, which means the leaves are located at the tip of thebranch. The bark of Terminalia plants usually has cracks and branches tucked into layers.Most of the Terminalia plants’ leaves are large, leathery with solitary or clustered smallgreen white fowers. Their fruits are yellow, dark red or black; drupe, usually angular or winged. Some fruits are edible, highly nutritious and have medicinal values [1]. Terminalia species are widely distributed in the southern Asia, Himalayas, Madagascar, Australia, andthe tropical and subtropical regions of Africa. Terminalia plants in southern Asia have beenintensively studied

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phytochemically due to their wide usage in Asian (India, Tibetan, andChinese) tra-ditional medicine systems.

Terminalia bellerica commonly known as bibhitakinbelongs to the family Combretaceae. *Terminalia bellerica* Roxb. Is one of the ingredients of ayurvedic purgative medicament of 'Triphala' available in the Indian market for the treatment of dyspepsia, diarrhea, and dysentery, inflammation of the small intestine biliousness, flatulence, liver disease and leprosy. Chemically, the presence of β-sitosterol, gallic acid, ellagic acid, galactose, ethyl gallate, chebulagic acid, mannitol, glucose, galactose, fructose and rhamnose in the fruit of *Terminalia bellerica* have also been reported. Active principle such as gallic acid (3, 4, 5-trihydroxybenzoic acid) has also been identified. It shows marked bile stimulating activity and has strong antioxidant properties. This review was mainly sites the information on highlight the phytochemical profile and bioactivities of *Terminalia bellerica* plant.

Fig.1:Terminalia bellirica-leaves

- ***MORPHOLOGY***

Terminalia bellirica, typically grows to a height of 20 to 35 meters, with a straight trunk that can measure up to 2 meters in diameter. The leaves of *T. bellirica* are simple, alternate, and broadly ovate, measuring about 10 to 15 cm in length and 7 to 10 cm in width. They have a glossy surface with a rounded or heart-shaped base, and the leaf margin is smooth. The leaves are arranged in a spiral pattern towards the ends of branches, creating a dense canopy. Flowers of *T. bellirica* are small, yellowish-white, and arranged in spikes that are about 10 to 15 cm long. These flowers are bisexual, meaning they contain both male and female reproductive organs. The flowering season generally occurs from April to June. The fruit is a distinctive feature of *T. bellirica*. It is a drupe, oval or ellipsoid in shape, and measures about 2 to 4 cm in length. The fruit is green when unripe and turns a yellowish-brown or greyish color upon maturity. The surface of the fruit is covered with fine, velvety hairs. Inside the fruit is a single, large seed that is hard and dark brown.

Fig.2: Dried Baheda chilka

Traditional uses

Fruits are laxative, astringent, anthelmintic and antipyretic useful in hepatitis, bronchitis, asthma, dyspepsia, piles,diarrhoea, coughs, hoarseness of voice, eye diseases andscorpion-sting; used as a hair tonic. Decoction of the greenfruit is used for cough. Pulp of the fruit is useful indysenteric-diarrhoea, dropsy, piles and leprosy. Half ripefruit is used as purgative. Kernel of the fruit is narcotic.Fruits are used in menstrual disorder in Khagrachari. Seed oilis used in rheumatism. Gum of the bark is demulcent andpurgative. The triterpenoid present in the fruits possesssignificant antimicrobial activity. Kernel oil has purgation action and its prolonged use was well tolerate[2].

Phytoconstituents

Glucoside (bellericanin) Gallo-tannic acid, Coloringmatter, 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 andchebulagic acid, phyllemblin, β-sitosterol, mannitol, glucose,fructose and rhamnose.

Pharmacological effects

Analgesic activity: ArifUllah Khan (2010)describes the antisecretory and analgesic activities of the crude extract of *Terminalia bellerica*. *T. bellerica* extract atthe dose range of 300 - 1000 mg/kg

inhibited the castor oilinducedintestinal fluid secretion in mice. The extract alsodose-dependently (50 - 100 mg/kg) where it reduced thenumbers of acetic acid-mediated in mice. These resultsindicate that *TB* exhibit antisecretory and antinociceptiveeffects, hence justifying its medicinal use in diarrhea and pain.

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

Antihypertensive Effect: Arif Ullah Khan (2008)was screened the effect of TB in hypertension. After administration of TB, they observed that fall in the arterialBP of rats under anaesthesia. In isolated guinea-pig atria,inhibition of force and rate of atrial contractions noted. Inrabbit thoracic aorta, relaxation was observed after theinduction of contractions which was induced byphenylephrine.

Anti salmonella activity: Madani (2008) werestudied the effect of T. *belerica* against *Salmonella typhi* and*Salmonella typhimurium*. *In vitro* cellular toxicity alsoperformed by them. In this study, Petroleum ether, chloroform, acetone, alcohol and aqueous extract of TB fruittaken for screening. When compared with other extractsbothalcoholic and aqueous extracts of TB showed significantanti-salmonella activity. There was no cytotoxicity wasobserved in *in vitro* cellular toxicity study.[3]

Anti-microbial activity: Elizabeth K M (2005)were conducted the antimicrobial activity of TB againsthuman microbial pathogens. The Aqueous extract of dry fruitat 4 mg concentration showed highest zone of inhibitionagainst *S.aureus.* These pathogens were highly sensitive tothe methanol extract also except E. coli (enteropathogen) andP. aeruginosa. Finally they concluded that TB dry fruitpossesses potential broad spectrum antimicrobial activity .

Antimicrobial and Toxicity Studies: Badrul Alam (2011) postulated that the crude methanolic extract of thefruits of *Terminalia belerica* Roxb along with its variousorganic fractions elicited both *in vitro* and *in vivo* antioxidantactivity as well as antibacterial activity. Total antioxidantactivity, scavenging free radical, authentic peroxynitrite andreducing power assessment were performed. Finally theyconcluded that the EtOAc fraction elicited strong activity inall the model systems with moderate toxicity.

Antioxidant activity: Ramesh Kumar (2011)postulated that the crude aqueous extract of the fruits of *Terminalia belerica* Roxb have antioxidant properties sincethese contains enzymatic and non – enzymatic antioxidants,these can be very effective against microbes causing variousdiseases. *In vitro* assessment of the antioxidant activity ofethanolic fractions of both these plants to scavenge 2, 2-Diphenyl-1-picrylhydrazyl(DPPH) and highly reactivehydroxyl radicals showed that the semi pure compoundspresent in thefractions are useful potential source ofantioxidants and can be used in the therapy of diseases likecancer, coronary heart disease, ageing and any other diseaserelated to oxidative stress. These fractions being non-toxicshowed significant antioxidant activity at scavenging freeradicals. They also significantly scavenge hydroxyl radicalwhich is known to cause cellular damage.[4]

Wound healing activity: Saha (2011) postulatedthat the paste of *Terminalia belerica* Roxb have properefficacy on wound healing. Herbal paste preparation showedsignificant (P<0.05) improvement on maturation, woundcontraction and epithelialization. Therefore it may beconcluded that the paste obtained from *Terminalia belerica*offers a distinctive advantage in wound healing.

Immunological activity: Aurasorn Saraphan chotiwitthaya *.postulated that T. bellerica* extract affected T cell proliferation mainly through the same mechanism asPHA. The extract with LPS and PWM also affected B cellproliferation through T cell-independent and T celldependentmechanisms respectively. The results indicatedthat the extract affected cellular mediated immunity (CMI)rather than humoral mediated immunity (HMI) .

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Acute and Sub-acute Toxicities: Thanabhorn S. (2009) were conducted acute and sub-acute toxicity studiesas per the OECD guideline. Single oral administration of theethanolic extract of T. *belerica* at a dose of 5,000 mg/kg didnot produce any toxicity. In sub-acute toxicity, repeatedadministration of 1,000 mg/kg of T. *belerica* over 14 daysdid not cause changes in terms of general behaviours ,mortality,weight gain, hematological or clinical blood chemistry parameters.The results of histological examinations showed normal appearance of the internalorgans when compared to those of the control group .

Immune response *In vitro:* *In vitro* Phagocytic activityand lymphocyte proliferation assay were carried out in
methanolic extract of on the mouse immune system(Aurasorn Saraphanchotiwitthaya 2008). In both assay,stimulation of macrophage phagocytosis and maximal activation of phytohemagglutinin were observed. Finally, theauthors concluded that the methanolic extract of T. *belerica*affected the mouse immune system, specifically both thecellular and humoral immune response *in vitro* .[5]

Hepatoprotective activity: Sangeetha Shukla *et al*,(2006) were evaluated the protective effect of TB fruit extract and its active principle, Gallic acid against CCl4intoxication. Treatment with extract (200, 400 and 800mg/kg, p.o.) and gallic acid (50, 100 and 200 mg/kg, p.o.)showed dose-dependent recovery in biochemical parameterssuch as SGOT, SGPT and lipid peroxidase, glutathione butthe effect was more pronounced with gallic acid.

Antibiofilm Activity: The ethanolic extract of a plant*Terminalia bellerica* (common name = Baheda) was testedfor its antimicrobial activity against the oral plaque formingbacteria *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 theformation of biofilm by the bacteria. The study suggestspossible benefits of this herbal preparation which inhibit thebiofilm 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 linestested. Synergistic effects (CI < 1) for *P.emblica*/doxorubicin or cisplatin at different dose levels weredemonstrated in A549 and HepG2 cells. The *T.bellerica*/cisplatin or doxorubicin also showed synergisticeffects in A549 and HepG2 cells. In some instances, thecombinations resulted in antagonistic effects. The dosereduction level was different and specific to eachcombination and cell line .[6]

β-lactamase inhibitor activity: The β-lactamaseinhibitor activity of 68 extracts from Indian herbs and spices was surveyed. Most promising results of the β-lactamaseinhibitor activity in*vivo* and *in vitro* were achieved from theherbal 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 ethanolicextract of *Terminalia belerica* (Combretaceae) fruits ETB was investigated in pylorus ligation and ethanol inducedulcer models in wistar rats. In both models the commonparameter determined was ulcer index. ETB at doses of250,500 mg/kg orally produced significant inhibition of thegastric lesions induced by Pylorus ligation induced ulcer &Ethanol induced gastric ulcer. The extract (250 mg/kg & 500mg/kg) showed significant (P<0.05) reduction in free acidityand ulcer index as compared to control .

Antithrombotic and Thrombolytic activity: An *invitro* model was used to check the clot lysis andantithrombotic effect of *Terminalia belerica* fruits along withStreptokinase as a positive control. From this study it wasfound that after addition of Streptokinase clot formation isdelayed upto more than 90 min whereas after addition of testsolution it was found that as the concentration of extract wasincreased the delay in clot formation also increases. At 0.20mg/dl concentration it showed the maximum delay (morethan 90 min.) in clot formation. For thrombolytic activity, atconcentration

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1.00 mg/dl the clot dissolution time isminimum i.e. 58 and66 min for aqueous and alcoholic extracts respectively .[7]

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

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

Materials and Methods

Chemicals

All the chemicals used in this study were analytical gradereagents with highest purity. The chemicals such as thiobarbituricacid (TBA), 5,50-dithiobis-2-nitrobenzoicacid (DTNB), pyrogallol, 1-chloro-2,4-dinitrobenzene(CDNB) and glutathione (GSH) were purchased fromSigma Chemical Co. (St. Louis, MO, USA). All the otherreagents were procured from Sisco Research Laboratories,156 Ind J Clin Biochem (Apr-June 2019) 34(2):155–163Mumbai, India. All the solvents used in the study werepurchased from Merck, India.[8]

Plant Material

Current season's fruits of T. bellirica were purchased fromKerala Forest Research Institute (KFRI), Peechi, India. Thefruits were de-seeded and dried in shade for few daysbefore made into fine powder. The fruit powder stored inair tight containers was used for the preparation of the
extract.

Preparation of Extract

Fruit powder of T.bellirica was extracted with 70% aqueousacetone in a mechanical shaker for 72 h after removingthe fatty substances by treating with petroleum ether. Afterevaporating the solvent completely, the extract was filteredand lyophilized to get in the powder form. The driedextract was kept in the refrigerator at 4°C till further use.

Experimental Animals

The male Wistar albino rats of 120–150 g, used in thestudy were purchased from the licensed breeder inKerala, India (Nagarjuna Herbal Concentrates Private Limited,T hodupuzha).The animals were acclimatized to the laboratory conditions for 1 week prior to the experimentation.Theanimals were housed in polypropylene cages, maintainedon a 12-h light/dark cycle at a temperature of25 ± 2 _C and provided standard pellet diet and waterad libitum. The studyprotocolmade in accordance with theCommittee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) guidelines (Reg NoB23032014-02) was approved by the Institutional AnimalEthics Committee of School of Biosciences, MahatmaGandhi University, Kottayam. All the procedures in theexperiment were carried out humanely.[9]

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Biochemical Parameters of Liver Function

The blood collected in clot stimulating tubes were kept inroom temperature for 30 min to separate the serum. Theserum was transferred to fresh tubes and stored at - 20 _Cuntil use. The serum samples were used to determineenzyme as well as other biochemical markers of liverfunction including aspartate transaminase (AST), alaninetransaminase (ALT), gamma glutamate transaminase(GGT), alkaline phosphatase (ALP), lactate dehydrogenase(LDH), total bilirubin, total protein, levels of albuminand globulin and albumin/globulin ratio (A/G). All theassays were carried out in semi auto biochemical analyzer(Microlab-ARX-235) using standard diagnostic kits (SpanDiagnostics Limited kits, Surat, India).

Hepatic Oxidative Stress Markers

A homogenate containing 10% liver tissue in 100 mMphosphate buffer containing 1 mM EDTA was used for allthe assays. The homogenate was centrifuged at 12,000 gfor 30 min at 4 _C and the supernatant obtained was usedfor the analysis of reduced glutathione (GSH) ,superoxide dismutase (SOD) and catalase (CAT) .[10]

Determination of Lipid Peroxidation and Nitric Oxide Levels

The levels of lipid peroxidation (LPO) and nitric oxidelevel (NO) was determined using liver homogenateand serum respectively.

Level of Reactive Oxygen Species (ROS)

The quantification of reactive oxygen species (ROS) contentin the tissue was determined according to the methodof] to assess antioxidant status of the liver tissue.[11]

Histological Evaluation of Liver

Hepatic tissue was dissected, washed in ice cold saline, fixed in 10% formalin, processed and embedded in paraffin. Tissue sections were prepared (5 lm thick), stained withhemotoxylin and eosin (H&E) and observed under microscopefor histopathological studies. Histopathological scoring was perfomed.[12]

Results

Polyphenol Composition of TBE by HPLC Analysis. Todetermine the polyphenol composition of TBE, we performedHPLC analysis. According to the HPLC analyticot, contents of GA and EA in TBE solution (40 mg/mL)were 4.6 mg/mL and 0.16 mg/mL, respectively .Thus, the contents of GA and EA in TBE powder were calculatedto be 115 mg/g and 4 mg/g, suggesting that gallic acid is the major polyphenolic compound of TBE.

Effects of TBE and GA on Cell Viability in RAW 264 Cells.We first analyzed the effects of TBE and GA on the viabilityof RAW 264 macrophages by MTT assay. As shown inFigure 1(b), no cytotoxic effect was observed when cells wereexposed to TBE (100–400 μg/mL) or GA (11.5–46 μg/mL) for 8 h.

TBE Exerted Anti-Inflammatory Effect in LPS-StimulatedMacrophages. As the production of inflammatory mediatorsis a well-known response to LPS stimulation in macrophages,we examined the effect of TBE on inflammatory mediatorexpression. TBE significantly reduced LPS-induced mRNAexpression of TNF-α, IL-1β, IL-6, MCP-1, iNOS, and SR-A,as well as protein expression of iNOS and SR-A.NO production was also examinedbecause excessive NO production is associated with inflammatoryresponses. As shown in LPS caused aconsiderable release of NO, but TBE significantly decreasedthe level of NO production. To evaluate regulatory mechanismsof TBE on inflammatory signaling pathways, we analyzedits inhibitory effect on NF-κB and MAPK activation.[13-14]

Western blot analysis revealed that the nuclear translocationof NF-κB p65 and phosphorylation of NF-κB p65, p38, JNK,and ERK were increased by LPS. Treatment with TBEeffectively inhibited the nuclear translocation of NF-κB andphosphorylation of all these proteins, whereas TBE did notaffect phosphorylation of IκB

Effects of GA and EA on Inflammatory MediatorExpression in LPS- and Palmitic Acid-Stimulated Macrophages. The present HPLC analysis showed that TBEcontains GA and EA and that GA is the major polyphenoliccompound of TBE. Therefore, we assessed the effects of GAand EA in TBE on inflammatory mediator expression. LPS upregulated the expression ofTNF-α, IL-1β, IL-6, MCP-1, iNOS, and SR-A in macrophages.GA

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treatment significantly reduced LPS-inducedexpression of TNF-α, IL-1β, MCP-1, and iNOS as well asTBE, but EA had no effect. Similar to LPS, saturated fatty acidsuch as palmitic acid is known to exert proinflammatoryactivity in macrophages via TLR4.palmitic acid increased the mRNA expression of IL-1β andMCP-1, while TBE significantly suppressed the expressionof these genes and GA reduced IL-1β expression

TBE and GA Suppressed ROS Production in LPS stimulated Macrophages. Elimination of ROS production is important for controlling inflammatory response. To confirmthe antioxidant effects of TBE and GA in LPS-stimulated macrophages, we measured intracellular ROS production using CM-H2DCFDA. ROS production was greatly increased by LPS, showingobvious green fluorescence, while TBE and GA significantly suppressed the level of ROS production in adose-dependent manner.

TBE Enhanced the Antioxidant Defense System in LPSStimulatedMacrophages. The antioxidant defense system,such as antioxidant enzymes, is important for the suppressionof oxidative stress and inflammatory response. We found thatLPS had almost no effect on the mRNA or protein expression of HO-1, NQO1, and GCLM and decreased the expression ofcatalase. Treatment with TBE significantly upregulated theexpression of these genes and the protein expression of catalasein the presence of LPS Nrf2 translocationfrom the cytoplasm to the nucleus plays a key roleinNrf2activation and the transcription of antioxidant enzymes. LPS had no effect on the nucleartranslocation of Nrf2, while TBE increased Nrf2 proteinwithin the nuclear fraction. In addition, as previous reportssuggested that some protein kinases such as PI3K/Aktand AMPK are involved in Nrf2 translocation [15] weexamined the effect of TBE on Akt and AMPK pathways. Phosphorylation of Akt and AMPK was slightly increased inLPS-treated cells, but a significant level of Akt and AMPKphosphorylation occurred in cells treated with TBE.[16]

Effects of GA and EA on Antioxidant Enzyme Expressionin LPS-Stimulated Macrophages. We also analyzed the effects of GA and EA in TBE on antioxidant enzyme expression inLPS-stimulated macrophages. The impacts of TBE, GA, andEA on antioxidant enzyme expression is similar to the effectson inflammatory mediator expression, that is, TBE and GAsignificantly induced the expression of HO-1, catalase, NQO1, and GCLM, but EA did not affect the expression ofthese genes.

Blocking Nrf2 Signaling Attenuated the AntioxidantEffects of TBE and GA in LPS-StimulatedMacrophages.Nrf2, a major transcriptional factor regulating the expressionof antioxidantenzymes, is involved in the suppression of oxidativestress.[17] To confirm whether the antioxidant effects ofTBE and GA are mediated by Nrf2, we silenced Nrf2 geneexpression in RAW 264 macrophages. When Nrf2 siRNAwas transfected into cells, the level of Nrf2 expression wasdecreased by approximately 60% compared with cells transfectedwith NC siRNA . knockdown of Nrf2 significantly inhibited theincrease in mRNA expression of catalase and GCLM inducedby TBE and GA, without affecting the expression of HO-1and NQO1. These results show that Nrf2 activation accountsat least in part for the antioxidant effects of TBE and GA inour system.Involvement of PI3K/Akt and AMPK Pathways inAntioxidant Enzyme Expression by TBE. TBE is capable ofactivating Akt and AMPK in LPS-stimulated macrophages.To determine whether Akt and AMPK areresponsible for the increased expression of antioxidantenzymes induced by TBE, we used LY294002 (Akt inhibitor)and compound C (AMPK inhibitor).[16] TBE significantly induced the expression of HO-1, catalase,NQO1, and GCLM. However, treatment of cells withLY294002 and compound C resulted in significant inhibition of TBE-induced antioxidant enzyme expression, indicatingthat the antioxidant effect of TBE is largely dependent onPI3K/Akt and AMPK signaling.[18]

TBE Increased Antioxidant Enzyme Expression andImproved Kidney Injury in LPS-Shock Model Mice. As thepresent data indicate that TBE exhibits antioxidant andanti-inflammatory properties in LPS-stimulated macrophages,we assessed in vivo protective effects of TBE inLPS-shock model mice. As shown in Figure 9(a), TBE significantlyinduced the mRNA expression of antioxidantenzymes (catalase, NQO1, and GCLM) but tended to reducethe mRNA expression of inflammatory mediators (TNF-$\alpha$and IL-6) in kidney

tissues.histopathologicalexamination of kidney tissues from the LPS group showed severe lesions including interstitial hyperemia,inflammatory cell infiltration in glomeruli, and glomerularcapillary narrowing. In contrast, these kidney injury featureswere attenuated in the TBE-treated group. The score of interstitial hyperemia was 2.3 ± 0.3 in the LPS group and 1.8 ± 0.1.[19]

CONCLUSION

Balela is an herbal drug that has been used in Unanimedicine for generations to cure problems such as obesity, atherosclerosis, gastrointestinal disorders memory loss, greying hair, immune weakness, loss of eyesight, general weakness, ageing, and so on. Experimental research has shown that it hasanalgesic, anti-diarrheal, anti-microbial, antioxidant, antihypertensive, antipyretic, immunomodulator, and hepatoprotective properties. Using the vaster sources of traditional medicines, which have a longand proven history of treating a wide range ofailments, has recently become a focus of research. More research should be done on this plant to identifythe undiscovered element of it that could benefit mankind.

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