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REVIEW ARTICLE

A Review on the Biological Effects of some Natural Products

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Abstract

This review is a compilation of a number of preclinical studies of the natural products for their biological activities. Many natural products studied for their biological activities are either in the form of herbal formulations or plant extracts. They showed antihypertensive, antilipidemic, antidiabetic, antioxidant, antianxiety, hepatoprotective, and many other activities. Many post graduate and doctoral students took part in studying the biological activities of these natural products. This comprehensive review will give an impetus for young research workers to explore the possibility of more biological activities on these natural products for the future studies to combat diseases.

Keywords: Antioxidants, Hepatoprotective, Herbal Medicine, Ischemia Reperfusion, Natural Products, Type 2 Diabetes

1. Introduction

Present lifestyle diseases like diabetes, hypertension, obesity and coronary artery diseases attribute to be the main cause of death in the world. Though there are many synthetic drugs available for the alleviation of these diseases, these drugs themselves have many drawbacks. Therefore, it has become necessary to search alternate forms of therapy to combat these dreadful conditions. For ages many herbal formulations, crude extracts, herbomineral drugs are in the therapeutic armamentarium of traditional system of medicine. It has been found that theses natural products have many chemicals in them which have several therapeutic potentialities to cure diseases like hypertension, diabetes, atherosclerosis and many other heart ailments. These traditional medicines may augment the present conventional method of treatment with lesser adverse effects. In this review we have disseminated many biological effects of several natural products which might be useful for many diseases.

2. *Terininalia arjuna*, *Withania somnifera*, *Tinospora cordifolia* (Abana)

Abana is a herbomineral compound (Himalaya Drugs) which contains *Terininalia arjuna, Withania somnifera, Tinospora cordifolia* and many other useful plant extract. Many heart diseases are treated with Abana. Abana was found to have antihypertensive as well as antianginal effect. Though there was a report for its antihypertensive effect, experimental evidences are lacking to establish its antihypertensive effect. Two experimental models were used to study the anti-hypertensive effects of Abana[1]. In the first model, hypertension was induced by the treatment of deoxycorticosterone acetate (DOCA+NaCl 0.9%) in unilaterally nephractomised rats and Abana (3g/kg/day/) was administered for 3 weeks in these animals.

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In the second model Abana was treated in $CdCl_2$ (1 mg/kg/day i.p. for 2 weeks) induced hypertensive animals. In both the models of hypertensive animals Abana showed a significant dimension in the blood pressure suggesting a potent antihypertensive effects. Chronic administration of Abana reduced the vascular reactivity to noradrenaline in isolated aortic strip and portal vein in the hypertensive animals. Abana might alter the cation transport into the cell thereby causing an antihypertensive effects[1].

3. *Hemidesmus indicus*, *Hibiscus rosa-sinensis*

Hemidesmus indicus (HI) cell culture extract was studied for its hypocholesterolemic activity in normal and experimentally induced hypercholesterolemic rats. Hypercholesterelomia was induced by giving atherogenic diet for 60days[2]. The effect of HI (2,4,16 mg/kg /p.o.) for next 30-60 on various lipid profile in serum. Tissue and fecal matter were investigated on these rats fed with atherogenic diet. It was found that there was a significant lowering in the levels of lipid in serum, heart as well as liver of the animals fed with atherogenic diet and HI for 60 days. Cholesterol and phospholipids were significantly increased in feces of rats fed with high fat diet and HI. It is concluded that HI has hypolipidemic effect in rats[2].

Langendorff-perfusion method was used to study the cardio protective effect of root of *Hemidesmus indicus* and *Hibiscus rosa-sinensis* (HRS). Global ischemia (I) was induced for 30 min followed by 1 hour reperfusion (R). HI 0.09 g/liter was perfused 15 min before global ischemia. Ischemic reperfusion injury was assessed by reperfusion arrhythmias, and infarct size (TTC staining), ventricular developed pressure (LVdevP), HR (heart rate, the left), maximal rate of pressure development (+dP/dtmax) and left ventricular end-diastolic pressure (LVEDP) ventricular premature beats (VPB) and duration of ventricular tachycardia (VT). Initial perfusion of HI for 15 min did not change (LVdevP) and HR significantly as compared to the pre perfusion value. During reperfusion of HI after I there was a significant recovery of (LVdevP). There was also a significant recovery of (LVEDP) and (+dP/dtmax) at 40 min of reperfusion when compared to non-treated control. After ischemia reperfusion (IR), HI significantly reduced the VT, VPB, contractile dysfunction and reperfusion induced arrhythmia in rats[3]. Similar effect was observed when *Hibiscus rosa-sinensis* was subjected to the above mentioned study. However, the effect of HI was more significant in all above mentioned parameters as compared to HRS[4].

4. *Azadirachta indica* (Neem)

A novel experiment was carried to investigate the effect of neem seed (kernel) powder (NP250 mg/kg) and glibenclamide (2.5mg/kg) alone or in combination in alloxon induced diabetic rabbits. It was found that NP alone and its combination with glibenclamide (0.25 mg/kg) were able to reduce the serum lipid levels, blood glucose and activities of serum enzymes like alkaline phosphatase (alk P), acid phosphatase (acid P), lactate dehydrogenase (LDH), liver glucose 6-phosphatase (G6P) and HMG CoA reductase activity in liver and intestine in alloxan diabetic rabbits). It was found that the combination of NP and glibenclamide produced a greater change than when they were given alone. It is suggested that NP produce a significant anti diabetic and antihyperlipidemic activities[5].

5. *Spirulina platensis*

A study was conducted to explore the antioxidant effect of *Spirulina platensis* due to its nutritional and medicinal properties. It is blue green algae which contains Phycobiliproteins (phycocyanin and allophycocyanin). Lead was used to induce oxidative stress in the animals. Therefore, it was thought that a study can be initiated to explore the anti-oxidant effects of *spirulina* by inducing oxidative stress by the administration of lead. In the lead treated animal there was a significant increase in the levels of these lipid peroxidative products. When *spirulina* was administered along with lead there was reduction in the levels of all lipid peroxidative products (malondialdehyde, conjugated diene and hydroperoxide) in the liver and kidney suggesting an antioxidant role of this algae[6].

A further study was carried out to find a synergistic effect of *spirulina* with vitamin C and E for their antioxidant action in the lead induced oxidative stress.

When lead was administered along with vitamin E (50 IU/kg), vitamin C (800 mg/kg) or *spirulina* (1500 mg/kg) there was restoration of membrane bound enzymes as well as the lipids (cholesterol, triglyceride and phospholipid) in the animal tissues to normal levels while lead acetate alone increased the levels of the membrane bound enzyme and other lipids. This study has led to the conclusion that vitamin E, C when given along with *spirulina*, there was a significant synergistic antioxidant activity thereby protecting the organs from the lead-induced toxicity[7].

6. *Moringa oleifera*

Moringa oleifera has been shown to have many medicinal properties. The leaves are the potential source for antidiabetic and lipidemic activity[8]. A study was undertaken to investigate the hypolipidemic activity of the fruits of *Moringa oleifera*. A standard laboratory diet, hypercholesterolaemic diet and fruits of *Moringa oleifera* powder were prepared according to the method of Mehta et al 2003[8]. Fruits of *Moringa oleifera (*200 mg/kg/day p.o) or Lovastatin (6 mg/kg/day, p.o.) were fed to the rabbits for 120 days in banana pulp. Lipid profile (Serum LDL, VLDL, HDL, cholesterol, triglycerides and atherogenic index) were investigated in all groups of animals. The entire above mentioned lipid parameters were reduced in *Moringa oleifera or* Lovastatin group as compared to the control group. However, *Moringa oleifera* - or Lovastatin treatment increased or decreased HDL levels respectively in hypercholesterolaemic rabbits. Treatment with *Moringa oleifera or* Lovastatin reduced the lipid contents in aorta and heart. Cholesterol in feces was found to increase with *Moringa oleifera.* This study shows that *Moringa oleifera* may be potential agent for treating hyerlipidemic patients.[8]

7. *Bacopa monniera, Emblica officinalis, Glycyrrhiza glabra, Mangifera indica and Syzygium aromaticum* (DHC-1)

A study was designed to investigate the antioxidant properties of DHC-1(*Bacopa monniera, Emblica officinalis, Glycyrrhiza glabra, Mangifera indica* and *Syzygium aromaticum*) – a formulation developed by Himalaya drugs. Administration of DHC-1 (100 mg/kg/day, p.o.& 200 mg/kg/day,p.o)for 30 days reduced the levels of SGOT and SGPT. This effect might be due to the membrane stabilizing effect of DHC-1[9]. It was further shown that DHC -1 increased the levels of Superoxide dismutase (SOD) and Catalase (CAT) which are the potent antioxidant enzymes. Besides, DHC-1 caused the reduction in lipid peroxidation levels. All these studies focus on the antioxidant effects of DHC-1that possess main ingredients as mentioned above.

A further study was carried out on DHI-1 to investigate its protective effect on isopronaline induced myocardial infarction (MI) and cisplatin stimulated renal damage. It was found that superoxide dismutase and catalse levels in the serum were increased in the animals treated with DHC-1 along with isoprenaline or cisplatine as compared to the animals treated with isoprenaline or cistalin alone. It was further shown that heart and kidney of animals treated with isoprenaline or cispltin respectively along with DHC-1 caused a reduction in the lipid peroxidation products thereby prevented the damage to the heart and kidney[10].

8. *Curcuma longa* (Curcumin)

Curcumin has been shown to have many medicinal properties and several findings on cucumin suggest that it has a very promising activity against various forms of cancer. A study was initiated to explore the possibility of anti lipidemic activity of cucumin. Triton WR 1339 was used to induce hypercholesterolemia in rats. Intaperitoneal injection of Triton WR 133 caused an increase in total cholesterol and triglycerides in rats as compared to control animals. Curcumin (200 & 400 mg/kg) administration reduced the levels total cholesterol and triglycerides in triton induced hyper lipidemic rats[11].

An attempt has been made to investigate the effect of cucumin on experimentally induced nephrolithiasis. Nephrolithiasis was induced in rats by administering Ethylene Glycol (EG) and Vitamin D3 (Vit. D3) and the extent of damage to the kidney was judged by the hyperoxaluria and renal deposition of Calcium oxalate crystals. Elevated oxidative stress, urinary oxalate level and renal deposition of Calcium oxalate crystals

was reduced in the animals treated with curcumin. Nephrolithiasis is also characterized by the deposition stones in the kidney which got mitigated by curcumin[12].

Oxidative stress plays an important role in diabetes. Cucumin by virtue of antioxidant effect might be helpful in preventing vascular dysfunction which occurs in diabetes. A study was carried out in experimentally induced diabetic rats to establish whether curcumin has any role in preventing vascular dysfunction due to its antioxidant action. Chronic diabetes was induced in rats by injecting streptazotozin (DIA-CON) In the diabetic animals and non-diabetic control (ND-CON) curcumin (200 mg/kg,p.o.) was administered and blood pressure as well as blood glucose levels were found to be normal in both groups of animals. There was no change in SOD and catalase activity in both the groups. In DIA-CON there was an increase in the lipid peroxidation levels. In the ex-*in vivo* experiments, aortic strip obtained from the DIA-CON rats there was a decrease in Ach relaxation. There was a significant reduction in the lipidperoxidation levels in the animals (DIA-CON) treated with curumin. Aorta obtained from the animals at the early stage of diabetes, phenylephrine showed an increase in contractile response where as in the middle and later stage of diabetes the contractile response was significantly reduced. In the isolated aorta obtained from DIA- CON animals, curcumin treatment attenuated phenylephrine-induced contractile response whereas in the middle and late stage of diabetes, curcumin treatment did not alter the Phenylephrine-induced contractile response. There was a significant improvement of Ach induced relaxation of isolated aorta obtained from the DIA-CON animals treated with of curcumin but it did not restore it to normal. Curcumin significantly reduced lipid peroxidation with DIA-CON but did not alter significantly effect on superoxide dismutase, catalase, and reduced glutathione. Chronic diabetes (hyperglycemia) led to excessive production of free radicals due to which curcumin was not able to prevent oxidative stress and vascular reactivity during the late stage of diabetes. From this study it is concluded that curcumin might be helpful in protecting the endothelial dysfunction only in the early stage of diabetes but not in the later stage[13].

9. Curcumin & quercetin

Doxorubicin is well known to cause oxidative stress thereby causing cardiac toxicity. Therefore, it was thought to carry out an experimental study whether administration of free radical cavengers like curcumin in combination with quercetin have any role to play in mitigating the doxorubicin induced oxidative stress. It was found that doxorubicin (10 mg/kg,i.v.) significantly elevated the levels of serum LDH, CPK, SGOT, CPK, and lipid peroxidation, SOD, catalase, GSH and membrane bound enzymes. All the aforementioned serum enzymes and other parameters returned to normal levels when co administration of curcumin with quercetin given along with doxorubicin[14].

10. Curcumin with Vanadium complex

Vanadiun is a very well metal for its antidiabetic activity. A chemical complex of vanadium with cucumin was made by chemical reaction (bis[curcumino]oxovanadium BCOV) to study its anti-diabetic activity in non-diabetic (ND) and streptozotocin-induced diabetic (DIA) rats. In DIA rats there was an increase in blood glucose, serum lipid levels along with a rise in cardiovascular parameter like blood pressure. In the DIA rats when noradrenaline (NA) and Ach were injected intravenously there was a significant alteration in their pressor and depressor responses respectively. In DIA rats BCOV (0.05, 0.1 and 0.2 mmol/kg/day, p.o.) produced a significant reduction in blood glucose and lipid levels in the serum. The blood pressure and the response to NA were restored to normal in DIA rats when treated with BCOV. From the above study it is interesting to find that BCOV can reduce levels of the blood glucose, serum lipid and blood pressure thereby forming a good candidate as an antidiabetic drug having additional property of alleviating cardiovascular complications[15].

11. *Camellia sinensis* (Green tea extract)

Cisplatin a well-known drug for cancer is having high risk of causing renal toxicity. Still there are no agents to mitigate the renal toxicity of cisplatin. Therefore, a

study was carried out to investigate whether *Camellia sinensis (*Green tea extract) could decrease the cisplatin induced renal toxicity. When the extract of green tea leaves (25,50,100 mg/kg,p.o .) was given to the rats treated with cisplatin (3mg/kg,i.p.) there was a reduction in the levels urea, , blood urea nitrogen (BUN), creatinine and uric acid in serum as compared to the rats treated cisplatin alone. It was further found that green tea leaves restored the levels of SOD, catalase, GSH, membrane bound enzymes and reduced the levels of lipid peroxidation in the kidney of cispltin treated rats[16].

As mentioned above, doxorubicin, a novel drug for the treatment several forms of cancer, is a notorious agent in causing severe cardio toxicity by virtue of activating free radicals (Oxidative stress). There is no agent to antagonize the oxidative stress caused by doxorubicin. Therefore, a study was undertaken to find whether administration of the extracts green tea leaves could have any antioxidant effect on doxorubicin induced oxidative stress. Administration of doxorubicin produced several changes in cardiovascular parameter such as increased blood pressure, prolongation of ST interval, increase in the serum levels of lactic acid dehydrogenase (LDH) creatinine phophokinase (CK), SGOT and lipid peroxidation products. Simultaneous administration of green tea leaves (100 mg/kg / day p.o. for 28 days) exhibited a significant change in the levels of aforementioned cardiovascular parameters and lipid profile on doxorubicin (3 mg/kg, IP on days 1, 7, 14, 21, 28) treated animals. Green tea extract also increased the levels all antioxidant enzymes (SOD, Catalase, GSH) in doxorubicin treated rats indicting its anti-oxidant effect. Histopathological observation showed that green tea leaves corrected the myocardial damage caused by doxorubicin. This study exhibited that extract of green tea leaves may be beneficial in counteracting the toxicities produced with doxorubicin by virtue of its antioxidant effects[17].

Reduction of doxorubicin induced cardiac damage by extract of green tea leaves provided an impetus to study its effect on cardiovascular damages (myocardial infarction MI) caused by isoproteranol. The levels of levels of triglycerides (TG), total cholesterol (TC) and free fatty acids (FFA), (LDL), (PL) and very low density lipoprotein-cholesterol (VLDL-c) in both serum and cardiac tissue were elevated in the animals injected with ISO (200 mg/kg, s.c. for 2 consecutive days at an interval of 24 hrs.). Vitamin E is also supposed have good antioxidant effects. Therefore, a combination of Vitamin E (DL-α-Tocopherol acetate,100 mg/kg/day, p.o) and the alcoholic extract of green tea leaves (100 mg/kg/day, p.o.) were administered together for 30 consecutive days and isoproteranol was injected on day 29th and 30th day. With this combination there was drastic restoration of lipid profile in heart as well as serum suggesting a vital role of green tea leaf extract and Vitamin E in isoproteranol induced MI[18].

A study was undertaken to investigate the effect of the extract of green tea leaves on doxorubicin induced testicular damage. When doxorubicin (3 mg/kg i.p. on day 1, 7, 14, 21, 28) was given to rats there was a decrease in body weight, sperm count, serum testosterone and also reduction in the levels of antioxidant enzymes such as in SOD, catalase and reduced GSH as well as the membrane bound enzymes and an increase in LDH, CP, SGOT and lipid peroxidation products. When green tea extract was administered simultaneously with DOX there was restoration of all the above mentioned parameters. The histopathological changes produced by doxorubicin in the testes got reversed to normal by the administration of green tea leaves[19].

12. *Glycyrrhiza glabra, Emblica officinalis and Tinospora cordifolia* (Pepticare)

Pepticare, a herbomineral formulation has been in use of Ayurvedic medicine. It contains *Glycyrrhiza glabra, Emblica officinalis* and *Tinospora cordifolia*. This drug is used for many gastrointestinal disorders. The present study was undertaken to investigate gastroprotective effect of pepticare. Two models of experimentally induced ulcer were conducted as mentioned by Bafna and Balaraman[20]. Gastric secretion and gastric ulcers in pylorus-ligation and on ethanol-induced gastric mucosal injury in rats were ameliorated by the oral administration of pepticare (125, 250, 500 and 1000 mg/kg). The ulcer index was also reduced by the administration of pepticare. Volume and total acidity, and an increase in the pH of gastric fluid in pylorus-ligated rats were reduced in pepticare treated animals.

SOD, Catalase and GSH were also increased in the treated animals showing an antioxidant activity of pepticare[20].

13. *Momordica cymbalaria*

The ethanolic extract of roots *Momordica cymbalaria* (250 and 500 mg/kg) was investigated for its antiovulatoryd abortifacient activities. The extract produced an increase in metaestrous phase and proestrous phase but diestrous phase was unchanged in treated groups when compared to control. On histopathological examination it was found that the ovary showed an increase in preovulatory and atretic follicles. Obortificant effect of the ethanolic extract was also seen in pregnant rats and antiimplantation activity were seen with the ethanolic root extract of *Momordica cymbalaria* (500 mg/kg) There was no increase in uterine weight or vaginal cornification during estogenic activity. The ethanolic root extract of *Momordica cymbalaria* exhibited antiimplantation and obortificant activities[21,22].

The antidiabetic activity of *Momordica cymbalaria* was studied in two sets of experiments. In the first set, diabetes was induced by injection of STZ (65 mg/kg) in 16 hours the fasted animals. In the second set of experiments Fructose Rich Diet (FRD) for 15 days was fed to animals to induce hyperinsulinemia with diabetes. A decrease in serum glucose, triglyceride, cholesterol, levels and a significant increase in HMG CoA reductase liver glycogen and. serum insulin were observed in the STZ induced diabetic animals treated with saponin fraction of *Momordica cymbalaria.* In the second set of experiments when FRD fed rats was treated with saponins of *Momordica cymbalaria* there was a significant increase in the ratio of HMGCoA vs Mevalonate reversal of the atrophy of the pancreatic islets of β-cells with an increase insulin secretion, increases hepatic glycogen level and attenuation of hyperinsulinemia. All the aforementioned actions contribute to the antidiabetic effect of *Momordica cymbalaria*[23].

A study was carried out to establish the hepatoprotective effect of *Momordica cymbalaria.* Carbon tetrachloride induced hepatic damage was the model used for investigating the hepatoprotective effect of *Momordica. Momordica cymbalaria* (250, 500 mg/kg, p.o/14days) or silymarin (100 mg/kg p.o./14days) was administered to Wistar rats along with CCl_4 (1.25 ml/kg, ip/14days). Extract of roots of *Momordica cymbalaria* or silymarin showed a significant hepatoprotective action when the activity of serum AST, ALT, ALP, bilirubin, total protein, cholesterol, triglyceride hepatic lipid peroxidation was decreased. It was also found that various anti-oxidant enzyme levels increased in animals treated with *Momordica cymbalaria* or silymarin as compared to animals treated with CCl4 alone. *Momordica cymbalaria* (250, 500 mg/kg, p.o/14 days) or silymarin (100 mg/kg p.o./14 days) reversed the liver cells to normal parenchymal architecture with cords of hepatocytes, portal tracts and central veins without noticeable alterations. The hepatoprotective effect of *Momordica cymbalaria* might be due to the its antioxidant property[24].

14. *Trigonella foenum* (Fenugreek seeds)

Fenugreek seeds have been shown to have many medicinal properties in auyrveda[25]. A study was carried out to explore the possibility of these seeds to have any anti-hypertensive activity. Two hypertensive models[25] were chosen to find out the anti-hypertensive effects of Methanol Fraction (MF) and Methanol Extract (ME) of the seed. There was a significant reduction in blood pressure of DOCA salt animals when administered chronically with methanolic fraction (30 mg/ kg day p.o.). Methanolic extract (100 mg/ kg /day p.o.) reduced blood pressure in fructose-induced hypertensive rat. Vascular reactivity to various agonists like serotonin, noradrenaline, and adrenaline were reduced after completion of the treatment schedule of both models in rats. This study shows that fenugreek seeds has got the potentiality to reduce the blood pressure and even can be tried in human clinically without much side effects.

15. *Korean ginseng* extract

Anxiety has been of the dreadful disease prevailing in adults particularly in the pandemic conations

like covid-19. Though there are many drugs like benzodiazepines and they have many disadvantages like drug dependence etc. Therefore, there is need to have the alternate system of medicine which can provide some chemicals with less side effects. In this contest a study on extract of Korean ginseng (3, 10 and 30 mg/kg) or diazepam (1 mg/kg) on animals showed significantly increased the time spent in open arms of elevated plus maze, and the number of entries in open arms, increased the number of transitions in light/dark apparatus, increased the number of squares traversed in open field apparatus. Number of head pokes were significantly increased hole board apparatus**.** Korean ginseng extract did not affect the motor coordination. Thus anti-anxiety activity might be due to the saponin content of standardized Korean ginseng extract[26].

16. *Tinospora cordifolia, Rubia cordifolia*

Allergic disorders are more common in several skin diseases. Despite having many drugs, several skin problems are off immunological origin and becomes incurable. Therefore, there is a search for alternate form of therapy. *Tinospora cordifolia, Rubia cordifolia* were evaluated for their antiallergic activity in the experimentally induced allergic condition[27,28]. It was found that *Tinospora cordifolia* and *Rubia cordifolia* exhibited significant inhibition in vascular permeability, inhibition in histamine release from the rat conjunctiva. There was reduction in level of reduced level of histamine content in tears. Egg albumin-initiated experimental allergic conjunctivitis were inhibited by *Tinospora cordifolia* and *Rubia cordifolia*. *Tinospora cordifolia* reduced the histamine induced paw edema in mice and histamine induced bronchial asthma in guinea pigs. Compound 48/80 induced lethality in rats was inhibited by *Tinospora cordifolia* (125 to 1000mg/kg) dose-dependently. In addition, TNF-α was inhibited by *Tinospora cordifolia* in dinitrophenyl (DNP) IgE-stimulated rat peritoneal mast cells. All these experiments conclude that *Tinospora cordifolia, Rubia cordifolia* might be having potent antiallergic components[27,28].

17. Hesperidin

Myocardial ischemic reperfusion injury is commonly encountered in during treatment of MI. It has already been shown in this article that *Hemidesmus indicus* and *Hibiscus rosa-sinensis* were successfully employed in the experimentally induced ischemic reperfusion (I/R). Therefore, an attempt has been made to find out the effect of Hesperidin in I/R for its antiarrhythmic effects and on other markers of tissue injury. Hesperidin is present in oranges, lemon, grapefruit and tangerines. Hesperidin significantly increased in tissue nitrite, reduction in inflammation, increase in antioxidant levels as well as decrease in arrhythmias and apoptosis. Reduction in inflammation and oxidative stress, correction of I/R induced arrhythmias by hesperidin might be due to its anti-inflammatory as well as antioxidant action[29]. An experiment with renal ischemic reperfusion injury was carried out according to the method of Chintan Gandhi et al.[30]. An improvement in the renal dysfunction and reduction of inflammation and apoptosis after ischemia/reperfusion injury by hesperidin is important feature of this study. All these properties might be due to its antioxidant effect. These findings may have major implications in the treatment of human ischemic acute renal failure[30].

18. *Lagenaria siceraria*

Myocardial injury was induced by injecting isoprotereno l(200 mg/kg, s.c.) and various parameter like serum uric acid, tissue Na^{++} and Ca^{++} ions and membrane-bound Ca^{+2}-ATPase activity along with serum protein, tissue K^{+} ion, vitamin E were investigated. Lactate dehydrogenase isoenzyme level and histopathologic alterations in the heart are also evaluated. There was a significant cardioprotective effect of the *L. siceraria* fruit juice (400 mg/kg/day, p.o.) administration for 30 days on isoproterenol-induced myocardial injury in rats by virtue of altering aforementioned parameter to the normal levels[31].

19. Lycopene

Lycopene is one of the main red carotenoid constituents present in tomatoes and other fruits and vegetables such as red carrots, grape fruits etc. In isoproterenol

induced myocardial infarction, there was a significant increase in C-reactive protein, caspase-activity, nitrite levels and myeloperoxidase. In addition, there was an alteration in the levels of electrolytes, vitamin E, serum protein and uric acid. DNA fragmentation was seen in Gel electrophoresis of isoproterenol injected rats. There was an increase area of infarction shown in triphenyl tetrazolium chloride staining in isoproterenol injected rats. Lycopene significantly prevented the Isoproterenol induced alteration in ECG, haemodynamic, biochemical and apoptotic changes in rats[32].

20. *Euphorbia thymifolia*

Ghanshyam et al.[33] evaluated the antiasthmatic and antianaphylactic effect of *Euphorbia thymifolia* methanol and aqueous fractions on experimental animals. Anaphylactic activity was assessed using horse serum and triple antigen vaccine anaphylaxis model. These sensitized animals were treated with therapeutic dose of 250 and 500 mg/kg orally for 14 days. At the end of treatment, the asthma score, biochemical parameters like blood cell counts and IgE were measured from blood. Cytokines such as interleukin (IL)-4, IL-5 and TNF-α were estimated for serum using ELISA. Along with this histopathology of lungs was carried out. However, antiasthmatic effect was investigated using the histamine induced bronchospasm in guinea pigs. In vitro mast cell stabilizing action of fractions was checked rat intestinal mesenteric mast cells challenged by compound 48/80. The treatment with fractions ameliorate the asthma score, blood cells count and cytokines levels significantly. The fractions also showed the positive effect on as antiasthmatic action on guinea pig and significantly reduced degranulation of mast cells. This investigation concludes that the *E. thymifolia*can might be used as a potential antiasthmatic drug[33].

21. *Euphorbia hirta*

In the present study we investigated the antianphylactic, degranulation of mast cells and antiasthmatic action of *Euphorbia hirta* methanol and aqueous extracts on rodents. Anaphylaxis was induced by administration of horse serum and triple antigen vaccine as sensitizing agent in rats. The sensitized rats were treated with the therapeutic dose (250 and 500 mg/kg p.o. for 14 days). Upon completion of treatment with extracts asthma score, IgE, Interleukin (IL)-4, IL-5 and TNF-α were measured for BALF. Histopathological changes in lungs also checked. Antiasthmatic action of extracts was checked on guinea pig model. Degranulation of mast cells was checked on rat mesenteric mast cells challenged with compound 48/80. Result of the study drawn the positive response of the extracts on the blood cell counts, IgE and cytokine levels. Extracts significantly reduced the bronchospasm in guinea pigs. Additionally, extracts showed the significant reduction the mast cell degranulations in mesenteric mast cells. Hence, this investigation concluded that the *E. hirta* could be served as potential candidate in the treatment of asthma[34].

22. *Euphorbia thymifolia*

The aim of the current study was to check the hypoglycemic and hypolipidemic effect of aerial part of *Euphorbia thymifolia* methanol and aqueous extracts on experimentally induced type 2 diabetes in rats. The type 2 diabetes was induced by administration of STZ (65 mg/kg, i.p.) followed by NA (110 mg/kg i.p.) 15 min later. The animals were treated with therapeutic dose of extracts up to four weeks. At the end of the treatment the fasting blood glucose level, insulin, HbA1c along with serum lipid profile and renal profile were assessed. Upon treatment with extracts the results showed the significant changes fasting glucose level, insulin, HbA1c level, lipid profile and kidney profile. This study supports the traditional proclamations on *E. thymifolia* aerialparts[35].

23. *Vaccinium macrocarpon* (Cranberry)

Psychiatric disorders are difficult to treat since many patients do not respond to the presently availables drugs. Therefore, there is a need for altenate system of medicine which might be helpful in combating these illness effcetively in most of the patients. Previously *Rauwolfia serpantina* (Reserpine) was the only drug of plant origin available for the treatment of psychosis.

Reserpine is not being used presently due to its side effects and availability of better drugs. Few more agents of plant origin like St John's wort etc. were also available for the treatment of psychiatric disorders. Therefore, it was thought interesting to evaluate aqueous extract of cranberry (*Vaccinium macrocarpon)* concentrate against MK-801-initiated psychosis in mice. Administration of aqueous extract of cranberry at the dose of 1000 and 2000 mg/kg for two weeks in MK-801-initiated psychosis and numerous neuro-chemical biomarkers viz. glutamate, glycine, serotonin, nor-adrenaline, gamma-amino butyric acid, dopamine and oxidative stress parameters like nitrite levels along with behavior abnormalities were measured. MK-801 initiated psychosis animals exhibited a noticeable rise in loco-motor movement, immobility time in forced swim test alongside a substantial reduction of escape latency time in Cook's pole test, time of permanency in rota-rod test, whereas treatment with aqueous extract of cranberry showed a substantial alteration in aforementioned behavioral abnormalities. There was a substantial increase in serotonin, dopamine, nor-adrenaline and decrease in glycine, gamma-amino butyric acid and glutamate levels in the psychosis initiated by MK-801. However, aqueous extract of cranberry at both doses treated mice exhibited remarkably alteration in above-mentioned neuro-chemical biomarkers. Acetylcholineesterase, nitrite level and D-amino acid oxidase enzyme activity were significantly decreased in aqueous extract of cranberry treated mice. The study concluded that administration of aqueous extract of cranberry substantially ameliorated the behavioral symptoms by virtue of decreasing oxidative stress and neuromodulation[36].

24. Conclusion

The natural products are a big gold mine as a therapeutic armamentarium for several ailments. Now there is a need to explore their possible value as medicinal agents for the treatment of dreadful diseases. In the present scenario of covid-19, it has become mandatory to work extensively to find out a remedy from natural resources for this dangerous ailment which has taken a heavy toll on human beings.

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