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Mulberry (*Morus* spp.): A potential resource for medicinal value

VS Ramya, S Chandrashekhar and GN Ashoka

Abstract
The Mulberry (*Morus* spp.) originated from China, belongs to Moraceae, is an attractive high value crop and known for its unique flavour, aroma and its excellent nutritional and medicinal properties. Mulberry is typically a deciduous or medium sized woody perennial tree having upright fissured bark and cylindrical stem with a milky sap growing up to 10–13 m tall. Due to its chemical composition and pharmacological functions it has been extensively used to prevent and cure human diseases for more than a millennium in Asian countries. Because of low toxicity and good therapeutical performance, mulberry leaves, fruits, root and bark were given considerable attention in traditional Chinese medicine.

Keywords: Mulberry leaves, fruits, root bark, 1-deoxynojirimycin, medicinal properties

Introduction
Medical science has made incredible advances all over the globe. Overall mortality rate decreased, expectancy of life increased, a lot of new life saving drugs discovered which helps us to fight against several infectious and other diseases, and new advancement in the field of technology has boosted the capacity of modern science. In 1998, WHO incorporates a new global health policy "Health for All in the 21st Century" and set the goal to achieve health security, health equity, increased healthy life expectancy and to ensure access to essential quality healthcare for all. Modern medical sciences, despite so many achievements and progresses is still finding difficult to reach to every people and deal with ever increasing diseases and disorders. Still majority of world population mainly in developing and under developed countries does not have access to modern medicine and depends on the time tested traditional or alternative system of medicine, many of these system is much older compared to the allopathic medical wisdom.

Genus -*Morus*, Family- Moraceae. More than 20 species and several subspecies or varieties. Sole Food-Silkworm (*Bombyx mor*i L.)

Therefore, the major questions still exist –
1. Whether the goal has achieved?
2. Whether 'Health for All' can be possible without scientific integration of traditional herbal medicine in clinical practice?

In 2013, WHO developed and launched 'WHO Traditional Medicine Strategy 2014–2023' and emphasised to integrate traditional and complementary medicine to promote universal healthcare and to ensure the quality, safety and effectiveness of such medicine (Sen and Chakraborty, 2016) [17].

Mulberry plant is one of the conventional herbs used in medicine. Since time immemorial due to its chemical composition and pharmacological function, most parts of mulberry plants are used in Chinese medicine (Ramesh *et al.*, 2014) [14]. Where mulberry containing more nutrient and less anti-nutrient content and mainly 1-DNJ a key element playing as a medicinal source. Mulberry known as a sole food for silkworm *Bombyx mori* L. also being used in different activities.

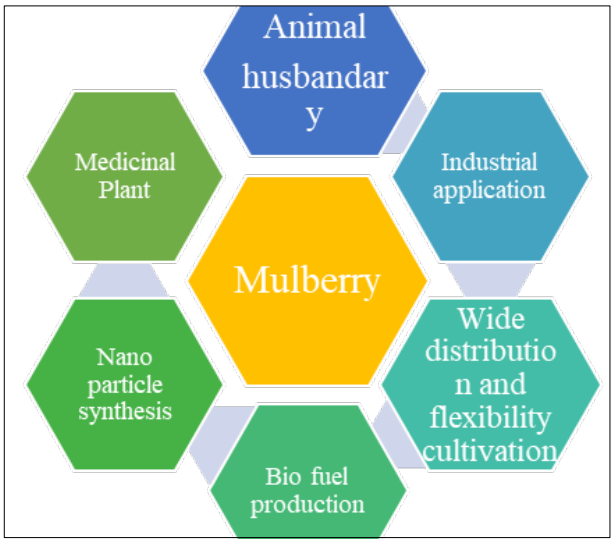

Fig 1: Mulberry in different practices

Nutritional importance of mulberry

Mulberry is a source of high value-added compounds, with nutraceutical application as functional ingredients, which include anthocyanin's, phenols, flavonoids, alkaloids, and other bioactive compounds (Table 1) hence this plant has remarkable effects in lowering serum glucose and blood cholesterol levels enabling their use in traditional Chinese herbal and folk medicines. Different parts of the mulberry, from the root bark to the leaves, have been extensively investigated for their various health benefits. Supplementation of foods with functional or bioactive ingredients has become an increasingly interesting way to develop new functional foods for health-conscious consumers. Enhancement of mulberry utilization has driven consumers to be more aware that a product can serve both nutrition and health promotion goals. This review focuses on the mulberry being used as "Anti" for diseases *viz.*, Blood glucose and lipid levels, Hyperpigmentation, Cancer cells, Ulcer, Venom and Wound healing.

Mulberry containing total phenolic, flavonoids, crude protein, crude fibre, total ash, minerals and also 1-Deoxynojirimycin (1-DNJ) can be said as a key element for all health benefits.

The various vegetative parts of mulberry are a subject of the incredible interest in the current scenario due to their amazing therapeutic properties. Mulberries have the unique characteristics to develop as a novel functional food due to their therapeutic properties and also a current topic of interest for many nutritionists. *Morus nigra* (Figure 1), *Morus rubra* have been emerged as most potential than the other mulberry species, as they exhibit maximum medicinal properties.

Mulberry fruits the major concern of the current scenario due to their excellent therapeutic properties and pharmacological relevance (Kumaresan *et al.*, 2008) [12]. The presence of phytochemicals and nutraceuticals in mulberries is responsible for a synergistic and diversified biological activities (Aggarwal *et al.*, 2004) [2] (Fig.2). Mulberry fruit juice can enhance the health by calming the nerves, promoting the metabolism of alcohol and immunity enrichment. Presence of different polyphenol contents in the mulberry fruits can treat many chronic diseases (Fig. 2). The consumption of mulberry fruit contributes overwhelmingly for the improvement of human health as they are a rich source of nutraceuticals including amino acids, carbohydrates, fats, vitamins, and minerals.

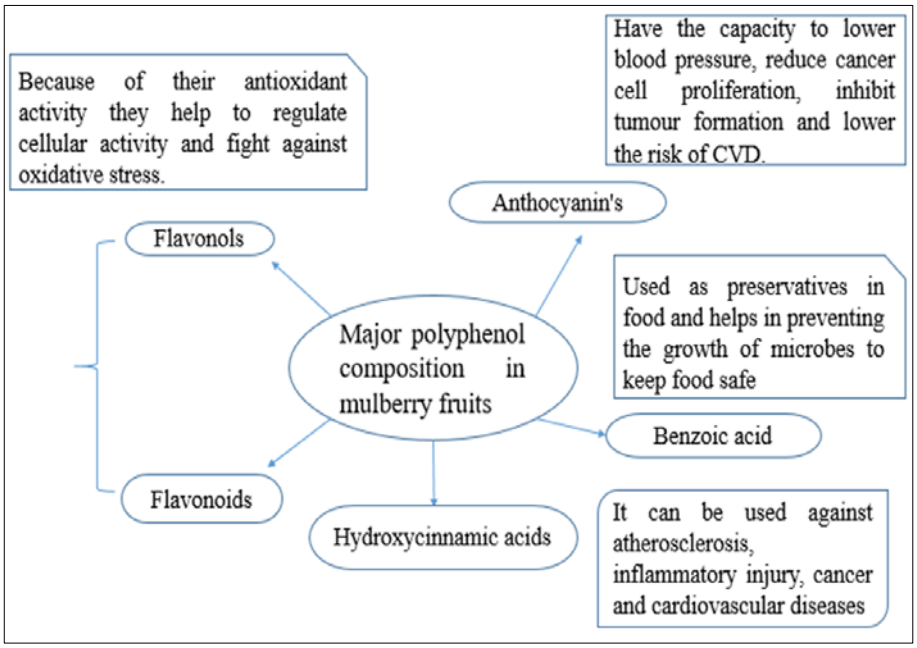

Fig 2: Major Polyphenol composition in mulberry fruits

Table 1: Nutrient content of mulberry

Nutritional Components and phytochemicals	Quantity
Total phenolic (TP)	8.76–20.26 mg Gallic acid equivalents (GAE) per g dry weight (dw)
Total flavonoid content (TF)	21.36–56.41 mg rutin equivalents (RE) per g dry weight (dw)
Total soluble sugars (TSS)	58.71–150.31 mg per g dry weight (dw)
1-Deoxynojirimycin (1-DNJ)	0.20-3.88 mg per g
Caffeoyl quinic acids	6.78-8.48 mg per g dry weight (dw)
Total soluble carbohydrates	3.1 g per 100 g fresh weight (fw)
Reducing sugars	1.5 g per 100 g fresh weight (fw)
Fructose and glucose	0.3 g per 100 g fresh weight (fw)
Sucrose	1.1 g per 100 g fresh weight (fw)
Crude proteins	15.31-30.91%
Crude fat	2.09-7.92%
Crude fibre	9.9-13.85%
Neutral dietary fibre	27.6-43.6%
Total ash	11.3-17.24%
Ascorbic acid	100-200 mg per 100 g
Beta-carotene	8.44-13.13 mg per 100 g
Oxalates	183 mg per 100 g
Phytates	156 mg per 100 g
Tannic acid	0.13-0.36%
Iron (Fe)	19-50 mg per 100 g
Zinc (Zn)	0.72-3.65 mg per 100 g
Calcium (Ca)	786.66-2,726.66 mg per 100 g
Phosphorus (P)	970 mg per 100 g
Magnesium (Mg)	720 mg per 100 g

1. Deoxynojirimycin as a source for mulberry medicinal value

Mulberry leaves are relatively rich in azasugar (Azasugars are alkaloids that mimic the structures of Monosaccharides). In azasugar, the oxygen atom in the ring of these sugars is replaced by nitrogen *viz.*, DNJ, Fagomine, N-methyl-DNJ are azasugars present in mulberry. DNJ is a 5-amino-1,5-dideoxy-D-glucopyranose or D-glucose analog (Fig.3), initially, DNJ was chemically synthesized by reduction of nojirimycin (Inoue *et al.*, 1967) [9], later, naturally occurring DNJ was isolated from the roots of mulberry trees and called moranoline (Yagi *et al.*, 1976) [23].

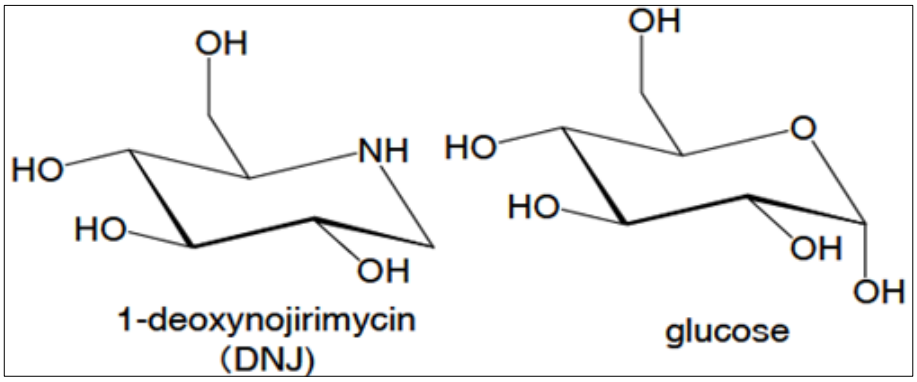

Fig 3: Chemical structure of DNJ and glucose

Carbohydrates ingested as food are digested to disaccharides by salivary and pancreatic amylases. The disaccharides are then hydrolysed to Monosaccharides by α-glucosidase at small intestine brush border and absorbed into blood (α-glucosidase is involved in this final step of carbohydrates digestion to absorption).

DNJ blocks the α-glucosidase activity which affect the conversion of disaccharides into Monosaccharides, therefore disaccharides cannot be digested as well as absorbed into intestine and eventually excreted. Thus decreases glucose absorption and lowers blood sugar level.

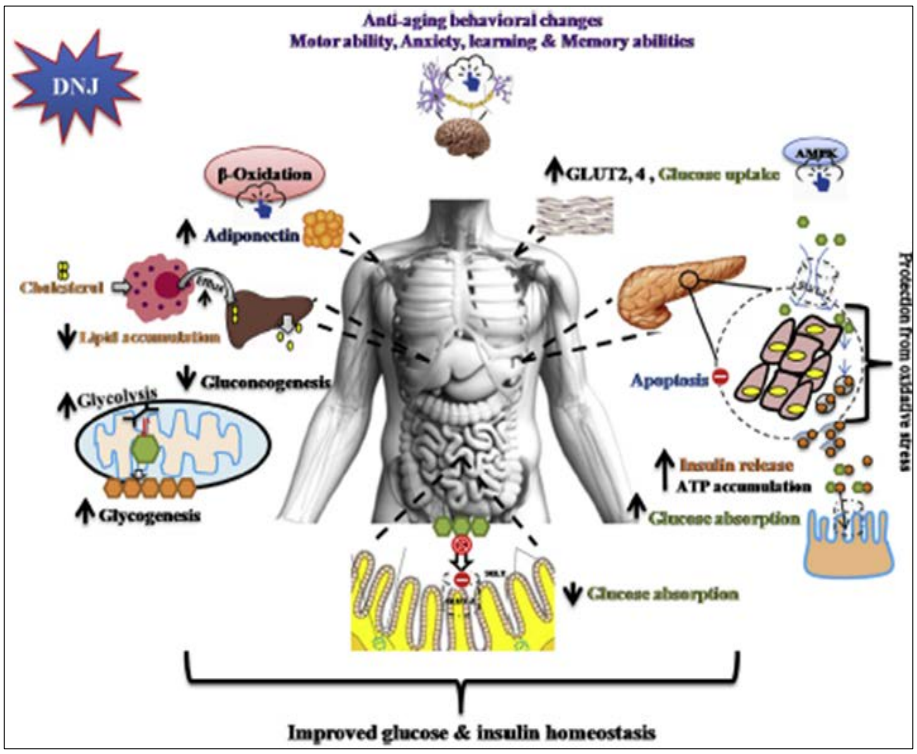

Fig 4: Schematic diagram for proposed mechanism of DNJ intervention and its multifaceted health benefits for regulation of various metabolic disorders

By taking DNJ in human body it helps in the following activities (Fig 4):

- **Increases adiponectin content:** It is a fat derived hormone. DNJ helps to protect against insulin resistance, diabetes and atherosclerosis. Decrease in adiponectin results in type 2 diabetes, obesity and cardiovascular diseases.
- **Decreases Lipid accumulation:** DNJ helps to decrease because for balancing the liver function, increase may lead to fatty liver.
- **Decreases gluconeogenesis:** It is a synthesis of glucose using pyruvate, lactate, glycosol and amino acid by hepatocytes. Increase may lead to diabetes and obesity.
- **Increases glycogenesis:** It is a glycogen synthesis, excess glucose produced in the body is stored as glycogen, it is activated by insulin in response to high level of glucose levels.
- **Increases glycolysis:** It is a cytoplasmic pathway which breaks down glucose into two to three carbon compound to generate energy. It occurs whenever there is a high concentration of glucose in the body. Thus glycolysis lowers the glucose levels by increasing removal of glucose from blood stream to most body cells.
- **Increases insulin:** Pancreas produces more insulin to compensate for the rise in blood sugar level, because insulin resistance may lead to type 2 diabetes.
- **Decreases glucose absorption:** The absorbed glucose is released into blood stream and is used for energy, thus increase may lead to diabetes.
- **Increase in Glut2, 4:** It is insulin regulated glucose transporter, it is responsible for insulin regulated glucose uptake into fat and muscle cells.

Blood lipid profiles

A pattern of lipids in the blood. Increase in lipid profiles cause fat deposits in your artery walls, risk for heart diseases.

Normal range

Total cholesterol: < 200 mg/dL.

HDL: 45 mg/dL- it is a good cholesterol; it carries cholesterol from other parts of body back to liver.

LDL: 100-129 mg/dL- it is a bad cholesterol; it leads to a build-up of cholesterol in arteries.

CM-TG: ultra-low density lipoproteins- it carry very little cholesterol but a lot of another fat (TG) so it is bad.

Fasting blood glucose: < 100 mg/dL, if it >100- 125 mg/dL pre-diabetic, >126- diabetes.

***Morus* spp. acting as 'ANTI' for different Diseases**

Kimura *et al.*, 2007 [10] conducted a study on food grade mulberry powder enriched with 1 DNJ suppresses the elevation of postprandial blood glucose in humans. In this study they selected twenty-four healthy volunteers to know the long-term effect of DNJ-enriched powder. After fasting for 12hours they were divided into four groups- control: given placebo (a substance has no therapeutic effect used for testing new drug), 1 DNJ enriched powder- 0.4 g, 0.8g and 1.2g followed by 50g of sucrose dissolved in 100ml of water before every meal for 38 days. Observations recorded at 0, 24 and 38 days of DNJ administration, 12 hours fasting blood was collected. The results revealed that glucose level has been decreased in group taken with DNJ enriched powder at 0.8 and 1.2g as time increases postprandial glucose level has been decreased and also conducted a study on food grade mulberry powder enriched with 1 DNJ suppresses the elevation of postprandial blood glucose in humans. In Fig 7. The results revealed that insulin level has been decreased in DNJ enriched powder taken group at 0.8 and 1.2g compared to placebo group and as time increases postprandial glucose level has been decreased.

Kojima *et al.,* 2010 [11] conducted a study to know the effect of mulberry leaf extract rich in 1 DNJ on blood lipid profiles in humans. For this study subjects were pre-treated for twice (before two weeks start of the study) and it was considered as baseline value. 1 DNJ rich mulberry leaf extract was given in a capsule form – 3 capsules daily for 3 times before each meal (9 capsules/day equal to 36mg/day) for 12 weeks, for control group placebo was given**.** The DNJ-rich mulberry leaf extract at a dose of 3 capsules three times daily before each meal for twelve weeks was given. The results revealed that the mean CM-TG (Chylomicron Triglycerides) was significantly decreased from baseline 18.6 mg/dl to 9.0 mg/dl at 12th week. The mean particle size of VLDL (Very Low Density Lipoprotein) was significantly decreased from baseline 47.03 to 45.92 and 45.87 nm at 6th week and 12th week, respectively. The LDL (Low Density Lipoprotein) was significantly increased from baseline 24.12 nm to 24.58 and 24.48 nm at 6th week and 12th week, respectively. The mean particle size of HDL (High Density Lipoprotein) was significantly increased from baseline 10.40 nm to 10.51 nm and 10.54 nm at 6th week and 12th week, respectively (Particle size of LDL is important role in congenital heart defects- if LDL is small and dense faces greater risk in congenital heart than with larger and less dense. Abnormalities in LDL structure is risk of cardiovascular diseases, hence use of DNJ mulberry leaf extract by improving plasma lipoprotein profile. Increase VLDL results in vascular cholesterol deposition because they are often oxidized and frequently induces adverse effect).

Banu *et al.,* 2015 [7] conducted a study on Reduction of postprandial hyperglycemia by mulberry tea in type 2 diabetes patients. Mulberry tea about 70ml was given to treated diabetic patients where control diabetic patients had normal tea. Fasting plasma glucose was taken early in the morning, later 90 minutes after taking tea postprandial glucose level was taken. The results revealed that postprandial glucose level has been decreased in mulberry tea taken group (210.21) compared to normal tea taken group (287.20). Thus mulberry leaf tea has the ability to decrease the postprandial glucose level in diabetes patients.

Taghizadeh *et al.,* 2017 [18] aimed to study the effect of mulberry leaf extract administration on markers of insulin metabolism lipid concentration and biomarkers of inflammation (HSCRP) and oxidative stress (Malondialdehyde) in patients with diabetic nephropathy (diabetic kidney diseases). Two groups were allocated 300 mg/day of mulberry leaf extract capsules and for control group – 300 mg/day of placebo for 12 week. The results revealed that after taking mulberry extract capsules for 12 week it had a favourable effect on different parameters. There was significant decrease in metabolic profiles *viz.*, Fasting plasma glucose level from baseline 137.6 mg/dl to 113.9 mg/dl, decrease in Triglycerides from baseline 179.8 mg/dl to 158.7 mg/dl, decrease in Very low density lipoprotein from 36.0 mg/dl to 28.5 mg/dl, decrease in biomarker of inflammation HSCRP from baseline 7.0 µg/ml to 4.7 µg/ml, where biomarker of oxidative stress Malondialdehyde remained constant 2.1 µmol/L. Increase in total antioxidant activity from baseline 1082.4 mmol/L to 1114.6 mmol/L (Total antioxidant activity (TAC) is used to assess the antioxidant status in biological sample against the free radicals produced in a disease. Increase in TAC decreases diabetes).

Mulberry leaf extract reduces the glycemic index of four common dietary carbohydrates (Wang *et al.,* 2018) [22], for this study they divided into seven groups from A to G, in A there were three members, From B – G each group has two members then experiment schedule were supplemented with different carbohydrates with and without mulberry leaf extract (MLE) at different visits. There were seven visits on different days. The results revealed that there were changes in blood glucose level of healthy persons after taking test food from 15 minutes to after 120 minutes when compared to glucose + MLE and glucose alone, in Maltose + MLE from 0.89 mmol/L to 0.13 mmol/L, Sucrose + MLE from 0.73 mmol/L to 0.20 mmol/L and Maltodextrin + MLE 0.73 mmol/L to 0.25 mmol/L, then it was also tested for Glycemic indexes of the test foods and of the carbohydrates without mulberry leaf extract the results revealed that food with Mulberry leaf extract showed low glycemic indexes reduction percentage in Sucrose + MLE was 33.51, Maltose + MLE was 53.11 and Maltodextrin + MLE was 31.0 when compared to glucose + MLE (8.12%) (Mulberry leaf extract had only a small effect on the absorption of glucose from gastrointestinal track because glucose is directly absorbed without requirement of α-glucosidase inhibitor. Hence a low glycemic index diet is widely recognized as playing a role in prevention and treatment of diabetes, MLE could be potentially used to decrease postprandial glucose level).

Aramwit *et al.* (2011) [6] conducted a study on Efficacy of mulberry leaf tablets in patients with mild dyslipidemia. The study was designed to check the cholesterol levels in non-diabetic with mild dyslipidemia because mulberry leaves have a potent hypoglycemic effect, using mulberry leaves in non-diabetic patients may initiate side effects due to low plasma glucose levels. About 280 mg mulberry leaf tablet three times a day before meals for 12 weeks (pre-prandial), observations were recorded on every fourth week for pill count and side effects. The results revealed that after 4th and 8th week there was no significant difference but after 12 weeks there was significant difference in total cholesterol from baseline 220.9 to 211.8 mg/dL, Low Density Lipoprotein from baseline 154.4 to 142.1 mg/dL and increase in High Density Lipoprotein from baseline 46.5 to 50.2 mg/dL but no significant decrease was observed in Fasting plasma glucose level (FPG) from baseline 90.5 to 87.6 mg/dL (No significant decrease in FPG may be due to water soluble fibre of mulberry leaves being with bile acid and being excreted in faeces, which intern leads to a decreased absorption of dietary cholesterol as well as lowered plasma and hepatic cholesterol.

Lee *et al.* (2002) [13] showed that Mulberroside F isolated from the leaves of *M. alba* L. inhibits melanin biosynthesis. From dried mulberry powder they extracted and isolated Mulberroside F (Compound I), where Kojic acid and phenylthiourea are used as positive control. This study revealed that the compound I at 100 µg/ml showed about 8.36% of Superoxide scavenging activity (Scavenging activity: A substance like anti-oxidant that helps to protect cells from the damage caused by free radicals. Tyrosinase: is the key enzyme involved in melanin biosynthesis, playing a role in Tyrosinase converts tyrosine directly into dopaquinine, and L-dopa is only produced from the recycling of dopaquinine). Where Kojic acid and phenylthiourea are used as positive control. The results revealed that highest dopa oxidase activity of tyrosine was recorded in compound I (Mulberroside F) at IC_{50} (0.29 µg/ml) with 51.6% inhibition

whereas, Kojic acid at IC_{50} (1.30 µg/ml) inhibited 98.6% activity, the results revealed that Compound I suppressed 50% of mammalian Tyrosinase activity at 68.3 µg/ml, where Kojic acid at 58.5 µg/ml showed strong inhibitory effect. The reduced production of melanin in Melan-a cells were about 30.6% in compound I and 46.7% in phenylthiourea, each at 1 µg/ml. Whereas, Kojic acid had no effect on melanin production of Melan-a cells at 1 µg/ml.

Akhtar *et al.* (2012) [4] investigated a study on Whitening and Anti-erythemic effect of a cream containing *Morus alba* L. extract. Treatments one was where fine powder of peeled mulberry root bark was added to emulsion known as formulation and without mulberry root bark it is base. Eleven male volunteers were selected for this study and each cream was marked as left or right for respective cheek and it was applied for twice during night for sixty days and observations recorded on first, second, third, fourth, sixth and eighth week. The results showed that melanin content was increased in base till the end of eighth week while formulation containing mulberry root bark extract decreased melanin content till the end of the study. It was also tested for erythema content where formulation decreased erythema content throughout study period compared to base. Thus mulberry containing phenolic compounds like anthocyanin and flavonoids which has Tyrosinase inhibitor activity in mulberry was useful for skin whitening and it is also a good source of ascorbic acid having inflammatory activities in mulberry decreased erythema content.

Ahmed *et al.* (2016) [3] studied the anticancer activity of *Morus nigra* L on human breast cancer cell line (MCF-7). The results revealed that the morphological changes of cancer cell line (MCF-7) treated with ethanolic fruit extract of fresh black mulberry at 100 µg/ml significantly exerted the antitumor activity about 40.0% of apoptotic than that of ethanolic fruit extract of dry black mulberry at 300 µg/ml (29.0%) after 48 hours compared to control group (1.0%) in giesma staining, the morphological changes of cancer cell line (MCF-7) treated with ethanolic fruit extract of fresh black mulberry at 100 µg/ml significantly exerted the antitumor activity about 27.7% of apoptotic than that of ethanolic fruit extract of dry black mulberry at 300 µg/ml (7.6%) after 48 hours compared to control group (1.0%) acridine orange/ethidium bromide staining, the MCF treated cells tested for total genomic DNA electrophoresis and results revealed that administration of fresh extract was significantly induced severe DNA damage which observed as a late stage of apoptosis with laddering pattern of DNA fragmentation after 48 hours of treatment compared to dry fruit extract and the cells were tested for comet assay (for detection of damage of DNA), after 24 hours of fresh fruit extract at 300 µg/ml administration cells showed significantly increase in percentage of damaged cells *i.e.*, apoptotic (22.4%), after 48 hours of treatment the results showed significantly elevation in percentage of DNA damaged cells (40.3%) when compared with dry fruit extract at 300 µg/ml 35.4% of damaged cells were noticed. It was also evaluated for mitotic index, the highest inhibition of mitotic frequency at 300 µg/ml of ethanolic fruit extract of fresh black mulberry was about (1.3%) after 48 hours of treatment, whereas, ethanolic fruit extract of dry black mulberry at 100 µg/ml exhibited the lowest inhibition index of 16.7%. All treatments illustrating the more effectiveness of anti-proliferative properties.

Turan *et al.*, 2016 [20] conducted a study on Anti-proliferative and apoptotic effect of *Morus nigra* L. extract on human prostate cancer cells. Mulberry fruits were air dried and converted into fine powder. PC-3 C and fibroblast cells were cultured in F-12k and Eagles minimal essential medium. Dimethyl sulfoxide extract of *M. nigra* L (DEM) at 0-1000 µg/ml and cisplatin at 0-1000 µg/ml. They are tested for different analysis that the cell cycle analysis after treatment with DEM at 370 0-1000 µg/ml and 666 0-1000 µg/ml increased at G0/G1 phase but it also decreased significantly at S phase (the first phase of cell cycle which DNA is replicated). (Note: Dimethyl sulfoxide can inhibit cancer cells invasion, migration, proliferation and colony formation through up regulation of HLJ1 (structure contribute to cancer progression) in a concentration dependent manner). The results also revealed that DEM at 370 µg/ml increased the number of early apoptotic and dead cells but it was not significant, where DEM at 666 µg/ml significantly reduced the number of viable cells and increased the dead, necrotic, late and early apoptotic cells.

[Mitochondrial membrane potential (MMP)

Cancer cells have more mmp because the nucleotide exchange is inversely oriented in mitochondrial inner membrane than normal cells. Mitochondrial membrane plays an important role in cancer cells through macromolecular synthesis and energy production. Tumours with pathogenic mitochondrial DNA mutation are benign in indicating the importance of respiration to cancer progression and it depletes ATP production**]**. The PC-3 cells also tested for mitochondrial membrane potential and results revealed that both concentration of DEM at 370 µg/ml and 666 µg/ml decreased significantly where DEM at 370 µg/ml showed reduction about 26.4% and 666 µg/ml showed reduction about 62.5%. Then there was increase in caspase 3/7 activity (are key mediators of apoptosis) where DEM at 250 µg/ml increased the activity about 3%, DEM at 500 µg/ml increased the activity about 11% and DEM at 1000 µg/ml increased the activity about 70% which was only significant.

Abdulla *et al.* (2009) [1] conducted a study on evaluation of the anti-ulcer activities of *M. alba* L. extracts in experimentally induced gastric ulcer in rats. The results revealed that the ethanolic leaf extract of *M. alba* at 500 mg/kg concentration had significantly reduced the gastric mucosal damage with ulcer area of 245.00 mm^2 compared to ethanolic leaf extract of *M. alba* at 250 mg/kg with ulcer area 485.00 mm^2. The reference anti-ulcer drug (omeprazole) at 20 mg/kg recorded ulcer area of 190.17 mm^2 and ethanolic leaf extract of *M. alba* at 500 mg/kg with ulcer area of 245.00 mm^2, both were found to be significant compared to negative control (10% Tween 80) with ulcer area of 1360.76 mm^2 control group has extensive visible haemorrhage necrosis of gastric mucosa but in *M. alba* L (500 mg/kg) treated gastric mucosa has mild microscopic necrosis due to cryoprotection of extract.

Abdulla *et al.* (2009) [1] conducted a study on evaluation of the anti-ulcer activities of *M. alba* L. extracts in experimentally induced gastric ulcer in rats. The results showed that in control group there is severe disruption of the surface epithelium ae seen and necrotic lesions penetrated deeply into mucosa with extensive edema of submucosa and leucocyte infiltration where as in *M. alba* L (500 mg/kg) treated group showed mild disruption of surface epithelium are present but deep mucosal damage is absent because the

extract reduced submucosal edema and leucocyte infiltration.

Chandrashekara *et al.*, 2009 investigated a study on Neutralization of local and systemic toxicity of *Daboia russelii* venom by *Morus alba* L. plant extract. Dried mulberry leaves (20 mg) dissolved in minimum amount of saline and used for neutralization studies. Mice were injected with venom in right foot pads in 20 µL saline and left foot pad with saline as control. For inhibition studies, venom was pre-incubated for 30 minutes with extract. The results revealed that *M. alba* L aqueous extract inhibited the caseinolytic activity of venom and the inhibition was found to be dose dependent. Venom: extract ratio 1:3 (w/w), fifty% inhibition was observed while at 1:7 complete inhibitions was achieved. The results revealed that Hyaluronolytic activity (to check the spread of toxins) results revealed that venom: extract at a ratio of 1:4 (w/w) showed fifty% inhibition and at ratio of 1:10 complete inhibition was observed. Edema activity showed that venom: extract at ratio 1:30 complete inhibition was observed. Myotoxicity (toxic effect on muscles) results revealed that venom: extract at a ratio of 1:20 the myotoxicity was inhibited to an extent of 98%, where presence of phospholipase A2 was responsible for induced myotoxic effect thus this study revealed that mulberry extract has the ability to inhibit phospholipase A2. The *M. alba* L extract was also tested for pro-coagulant activity and results revealed that venom: extract ratio at 1:20 the clotting time increased to four folds compared to control.

Evaluation of burn wound healing potential of aqueous extract of *M. alba* L. based cream in rats (Bhatia *et al.*, 2014 [8], Group 1- Sham control group: Animals in this group were just made to undergo the shaving procedure on the ear and then were kept undisturbed for the whole study protocol. Group 2 - Acute burn injury group: Animals were given scalding burn injury, according to a pre-devised method. 30 Animals were restrained in the rat holder and 5cm of the area on the back of the rats were carefully shaved to expose the skin. Boiling water was poured for 15 seconds on the exposed skin to induce full thickness burn. After the burn injury was induced, 0.8 mL of normal saline was given intraperitoneal to the animals to prevent spinal shock. Group 3 - Cream Base treated group: Animals were given scalding burn injury as discussed in Group 1. After the administration of saline solution, cream base (without any medicament) was applied on the affected area so as to cover the whole area. Group 4 - Silversulfathiazine (Standard Drug) cream treated Group: Animals were given scalding burn injury as discussed in Group 1. After the administration of saline solution, Silversulfathiazine cream (Silverex®) was applied on the affected area so as to cover the whole area. Group 5 -MA Extract based cream treated group: Animals were given scalding burn injury as discussed in Group 1. After the administration of saline solution, aqueous extract of *Morus alba* based cream was applied on the affected area so as to cover the whole area. The results also revealed that the wound contraction was significantly higher in the aqueous leaf extract of *M. alba* based cream treated group (84.6%) compared to that of cream based group without any medicament (43.6%). The mean period of epithelialization was found to be decreased significantly in the aqueous leaf extract of *M. alba* based cream treated group (12.1 days) compared to that of cream based group (19.6 days). It can be suggested that aqueous leaf extract of *M. alba* based cream exhibited better wound healing potential against thermal burn injury in rats.

Mulberry leaves (*Morus alba* L.) ameliorate obesity induced hepatic lipogenesis, fibrosis and oxidative stress in high fat diet fed mice (Ann *et al.*, 2015) [5]. After 12 hours of treatment mulberry leaf extract did not affect the body weight where High fat group increased weight from before treatment 34.30 to 48.35 after treatment but Low dose mulberry leaf extract (46.43) and High dose mulberry leaf extract (45.76) group did not affect vary when compared to HF group. The results also revealed that decrease in triglycerides in L (110.41) and H (103.22) group compared to HF (154.37), total cholesterol in L (135.16) and H (128.15) group compared to HF (167.77) and there was increase in High Density Lipoprotein cholesterol in L (82.24) and H (81.05) group compared to HF (60.43). Then it was also tested on hepatic function in high-fat diet-induced obese mice the results revealed that glutamic oxaloacetic transaminase and glutamic pyruvic transaminase activity were significantly reduced in L (117.07 Karmen/ml and 53.35 Karmen/ml) and H (117.07 Karmen/ml and 46.13 Karmen/ml) compared to HF group (200.84 Karmen/ml and 126.45 Karmen/ml) respectively, it also revealed that mulberry leaf extract at 666 mg/kg showed reduced fat accumulation n high fat diet induced obese mice. The results revealed that mulberry leaf extract group shows high thermogenesis in both UCP2 and PPARa which increases the energy expenditure and improves metabolism. Then mulberry leaf extract decreased the fibrosis (the formation of an abnormally large amount of scar tissue in the liver) in both collagen and a-SMA.

UCP2

Uncoupling protein 2-it plays a role in development of non-alcoholic fatty liver disease. It lowers redox pressure on mitochondria and acts against damage.

PPARa

Peroxisome proliferator activated receptor alpha- it is a family of nuclear receptor which regulates the expression of genes involved in fatty acid beta oxidation and regulates energy.

a-SMA

Alpha Smooth muscle actin it is a marker for a subset of activated fibrogenic cells.

Collagen

Fibrosis occurs when the synthesis of new collagen by myofibroblasts exceeds the rate at which it is degraded, such that the total amount of collagen increases overtime (increase in collagen may leads to side effects like bad taste, heartburn and fullness).

Conclusion

Population growth, rapid urbanization, environmental degradation and misuse of allopathic drugs are disrupting the equilibrium of the world. New diseases are emerging at unprecedented rate disrupting people's health and causing social and economic impact. The dependence on chemicals have been increased, awareness of the potential hazards for health and environment is required. Therefore, the world is looking for cost effective, easily available, better physiological, compatible traditional system of medicine and holistic approach to avert such problem and provide basic healthcare to all. Hence, mulberry can be effectively used as a

source of medicine since it is rich in phytochemicals in its different parts possessing different medicinal value for betterment of human and animal health.

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