Table 2-List of drugs selected for the proposed study

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Name of the drug</th>
<th>Family</th>
<th>Part used</th>
<th>Unani Name</th>
<th>Common Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td><em>Emblica officinalis</em> Linn.</td>
<td>Euphorbiaceae</td>
<td>Fruit</td>
<td>Amla</td>
<td>Amla</td>
</tr>
<tr>
<td>2.</td>
<td><em>Ammomum subulatum</em> Roxb.</td>
<td>Myrtaceae</td>
<td>Fruit seed</td>
<td>Heel Kalan</td>
<td>Bari Elaichi</td>
</tr>
<tr>
<td>4.</td>
<td><em>Cinnamomum cassia</em> Blume.</td>
<td>Lauraceae</td>
<td>Leaves</td>
<td>Sazaj</td>
<td>Cassia</td>
</tr>
<tr>
<td>5.</td>
<td><em>Coriandrum sativum</em> Linn.</td>
<td>Umbelliferae</td>
<td>Fruit</td>
<td>Kishneez</td>
<td>Coriander</td>
</tr>
<tr>
<td>7.</td>
<td><em>Crocus sativus</em> Linn.</td>
<td>Iridaceae</td>
<td>Stigma</td>
<td>Zafran</td>
<td>Saffron</td>
</tr>
<tr>
<td>8.</td>
<td><em>Santalum album</em> Linn.</td>
<td>Santalaceae</td>
<td>Heart wood powder</td>
<td>Sandal</td>
<td>Sandal</td>
</tr>
</tbody>
</table>

2.1. Amla (*Emblica officinalis* Linn.)

2.1.1. Pharmacological reviews

2.1.1.1. Effect on cardiovascular system and as antioxidant

Amla as has been shown to possess good antioxidant property alone as well as in combination with green tea, vitamins A, C and E (Jain *et al*., 2011; Kamal *et al*., 2011). Evaluation of amla in rodents has proved it to be ameliorative against increased lipid peroxidation as well as a decreased activity of enzymatic antioxidants and non-enzymatic antioxidants in both the organs (Chakraborty and Verma, 2010). Evaluation of its role against isoproterenol-induced cardiotoxicity showed cardioprotective potential attributed to antioxidant activity and favorable improvement in hemodynamic and contractile function (Ojha *et al*., 2011). Screening of hydroalcoholic lyophilized extract of drug against deoxycorticosterone acetate and high salt-induced hypertension showed modulating activity of endothelial nitric oxide synthase and prevention of development and progression of hypertension and cardiac hypertrophy (Bhatia *et al*., 2011). The antioxidant activity of amla can be attributed to its antioxidant potential (Chatterjee *et al*., 2011). The protective role of the drug was
studied in adult Swiss albino mice against arsenic induced hepatopathy and it significantly reduced arsenic induced oxidative stress in liver (Sharma et al., 2009).

2.1.1.2. Effect on CNS

Amla showed significant antidepressant-like activity probably by inhibiting MAO-A and GABA and also due to its antioxidant activity. Ascorbic acid and its constituents like flavanoids, tannoid principles and polyphenolic substances might be responsible for its antidepressant-like activity (Dhingra et al., 2012). The beneficial effects of Chyawanprash (contains amla as a major ingredient) have also been studied where it significantly protected the animals from developing memory impairment (Parle and Bansal, 2011). The hydroalcoholic extract of drug was studied against kainic acid-induced seizures, cognitive deficits and on markers of oxidative stress. Pre-treatment significantly increased latency of seizures as well as significantly improved the cognitive deficit induced by kainic acid (Golechha et al., 2011). The neuro-psychopharmacological effect of a polyherbal formulation containing amla as one of the ingredients on learning and memory processes showed significant decrease in transfer latency and also produced significant improvement in passive avoidance acquisition and memory retrieval (Shah and Goyal, 2011). Studies suggested, the potential of amla to be used as an adjuvant for treatment with antiepileptic drugs (Golechha et al., 2011). Oral administration of amla churna (an Ayurvedic preparation) produced a dose-dependent improvement in memory scores of young and aged rats. Its effect on memory was also carried out by measuring total serum cholesterol levels and brain cholinesterase activity in mice. It may be a useful remedy for the management of Alzheimer's disease on account of its multifarious beneficial effects such as memory improving property, cholesterol lowering property and anticholinesterase activity (Vasudevan, M., Parle, M., 2007a; Vasudevan, M., Parle, M., 2007b).

2.1.1.3. Effect on cancer

The pharmacological studies of the drug emphasized the aspects that warrant future research to establish its activity and utility as a cancer preventive and therapeutic drug in humans (Baliga and Dsouza, 2011). The studies showed that Triphala (Ayurvedic formulation containing amla as main ingredient) is useful in the prevention of cancer as well as possesses antineoplastic, radioprotective and chemoprotective effects.
(Baliga, 2010). Extracts of amla have showed good activity for colorimetric MTT assay (Penolazzi et al., 2008). The Pre-treatment with defatted drug extract showed significant partial recovery of pathological manifestations as compared to diethylnitrosoamine and 2-acetylaminoflourine treated rats and suppressed the tumor forming potential of 2-acetylaminoflourine. Hence, it can be said that the drug has the potential to suppress carcinogen-induced response in rat liver (Sultana et al., 2008). The growth inhibitory effect of the drug was assessed on human hepatocellular carcinoma and lung carcinoma cells. The synergistic effect with Terminalia bellerica extracts was also studied with doxorubicin or cisplatin. The drug extract showed growth inhibitory activity with synergistic effect (Pinmai et al., 2008).

2.1.1.4. Effect on liver

The aqueous extract of amla can significantly modulated the basal levels of oxidative markers and enhanced antioxidant defences of the cells using a hepatocyte cell line. The studies suggest that the hepatoprotective effects of the drug reported earlier may be largely due to its potential to enhance the antioxidant defences in vivo (Shivananjappa and Joshi, 2011). Mechanistic studies showed that the beneficial effects of amla in preventing the ethanol-induced hepatotoxicity are mediated by the antioxidant, free radical scavenging, anti-inflammatory and anti-fibrotic effects (Shivashankara et al., 2012).

The drug extract was studied using in vitro methods against alcohol-induced hepatic damage in rats. It was observed that, the drug possesses antioxidant activity and tannoid, flavonoid and nitric oxide scavenging compounds present in drug may offer protection against free radical mediated oxidative stress (Damodara Reddy et al., 2010). The drug was found to be more effective than vitamin C when it was studied on N-nitrosodiethylamine-induced injury in rats thus amla supplementation counteracts N-nitrosodiethylamine-induced liver injury via its antioxidant, anti-inflammation, anti-apoptosis and anti-autophagy properties (Chen et al., 2011). The oral administration of the drug extract on fructose-induced metabolic syndrome was assessed in rodents. It showed significant reduction in increased serum and hepatic mitochondrial thiobarbituric acid-reactive substance levels (TBARS) (Kim et al., 2010). The protective effect of the drug was studied on liver mitochondria of ethanol-administered rats where it offered protection by simultaneously lowering the carbonyl
content, lipid peroxidation and elevating antioxidant enzyme activities (Reddy et al., 2009). The ameliorative effect of aqueous extract of the drug was studied on ochratoxin-induced toxicity in the liver and kidney of mice (Verma and Chakraborty, 2008). A study was carried out for the hepatoprotective effect of the drug on isoniazid, rifampicin and pyrazinamide induced hepatic damage in rats. This study proved the synergistic protective effects exerted by the combination of the drug with Tinospora cordifolia when co-administered with anti tubercular drugs (Panchabhai et al., 2008). The effect of the drug has also been assessed against carbon tetrachloride (CCl₄) and thioacetamide induced changes in rat liver. The reversed such alterations with significant regenerative changes suggested the preventive role of the drug (Mir et al., 2007). The effect of prefeeding of dehydrated drug powder on hexachlorocyclohexane -induced changes on multicomponent antioxidant system and lipid peroxides in rat liver was studied and observed that the drug could decrease the formation of these lipid peroxides significantly (Anilakumar et al., 2007).

2.1.1.5. Antidiabetic effect

The fruit juice obtained from amla investigated on myocardial dysfunction in streptozotocin induced diabetes showed that it may be beneficial for the treatment of myocardial damage associated with type one diabetes mellitus (Reddy et al., 2011). The drug extract can significantly improved antioxidant defence in diabetic and atherogenic indices in uremic patients with diabetes (Chen et al., 2011). Anti-hyperglycemic and lipid-lowering properties of the drug in normal and diabetic human volunteers were assessed. The results showed a significant decrease in fasting and 2-h post-prandial blood glucose level in both normal and diabetic subjects. It also reduced total cholesterol and triglycerides level (Akhtar et al., 2011). The aqueous extract of the drug studied on targeted oxidative stress mediated nerve damage in diabetic rats. It significantly attenuated all the behavioral, biochemical and molecular alterations in a dose-dependent manner (Tiwari et al., 2011).

A study was carried out to explore the beneficial effects of the drug on acute pancreatitis induced by L-arginine in rats. The drug treatment was found to be beneficial for treating acute pancreatitis (Sidhu et al., 2011). The free radical scavenging capacity and antioxidant potential of different extracts of the drug were determined. Methanol extract of fruits exhibited maximum scavenging activity against
DPPH, superoxide, hydroxyl and nitric oxide radicals. Methanol extract was also screened for their antidiabetic activity via inhibition of $\alpha$-amylase, $\alpha$-glucosidase and antiglycation assays. Significant antiglycation activity also confirms the therapeutic potential of the drug against diabetes (Nampoothiri et al., 2011).

The drug was investigated against type II diabetes induced in male rats. The changes observed in lipid peroxidation status and anti-oxidant enzymes levels in diabetic rats were significantly recovered by the drug treatment (Kumar et al., 2009). The aqueous extract of the drug and its constituent tannoids inhibit Aldose reductase in vitro and prevent hyperglycemia-induced lens opacification in organ culture on diabetes induced in rats by streptozotocin. The results provided evidence that the drug and its enriched fraction of tannoids are effective in delaying development of diabetic cataract in rats (Suryanarayana et al., 2007).

2.1.1.6. Other activities

The supplementation of amla extract reduced the plasma oxidative marker and increased plasma total antioxidant status in uremic patients (Chen et al., 2011). The drug also possessed antidiarrheal and spasmyloytic activities (Mehmood et al., 2011) whereas it showed biphasic activity in ulcerated mice with healing effect against NSAID-induced ulcer (Bhattacharya et al., 2007; Chatterjee et al., 2011).

The drug extract exhibited potent antimicrobial activity against E. Cloacae, E. coli (Kumar et al., 2011) and Candida albicans (Thaweboon and Thaweboon, 2011). It also exhibited potent antibacterial activity against Escherichia coli, Klebsiella pneumoniae, K. ozaenae, Proteus mirabilis, Pseudomonas aeruginosa, Salmonella typhi, S. paratyphi A, S. paratyphi B and Serratia marcescens (Saeed and Tariq, 2007).

The drug extract showed in vivo antiplasmodial activity with good suppression (Pinmai et al., 2008) and anti-inflammatory activity against carrageenan induced rat paw edema and acetic acid induced peritonitis in mice (Dang et al., 2011). It can significantly reduce NO levels, erythrocyte membrane lipid peroxidation, C/P ratio, activities of Na$^+$/K$^+$, Mg$^{2+}$ ATPases and fluorescent anisotropic values in alcoholic rats (Reddy et al., 2009).

A study showed that, dietary supplementation with amla protects against Klebsiella pneumoniae colonization in lungs on long-term feeding (Saini et al., 2008).
Flavonoid-contents of the drug produced a dose-dependent and tissue-specific activation and inhibition effect on activity of mitochondrial ATP-dependent potassium channel (Mironova et al., 2008). The drug was found effective on the lipid metabolism and protein expression involved in oxidative stress during the ageing process. It may prevent age-related hyperlipidaemia through attenuating oxidative stress (Yokozawa et al., 2007).

2.1.2. Phytochemistry and analytical reviews

Sawant and co-workers (2010) reported a new, simple, sensitive, selective, precise and robust high-performance thin-layer chromatographic (HPTLC) method for the determination of gallic acid in dried amla fruit (Sawant et al., 2010). The volatile components and in vitro antimicrobial activities of essential oil obtained by hydrodistillation and supercritical fluid extraction were investigated and quantified by gas chromatography-mass spectrometry (GC-MS). The main components of both oils were beta-caryophyllene, beta-bourbonene, 1-octen-3-ol, thymol and methyleugenol (Liu et al., 2009).

The drug considered rich source of ascorbic acid and the antioxidant activities exhibited by the drug extract is superior to those of ascorbic acid itself. It is also having hydrolysable tannins emblicanins A and B, reported in the earlier literature, to be the contributory antioxidant molecules in the extract. The high content of ascorbic acid is also questionable due to previous non-identification of co-eluting mucic acid gallates. The high performance liquid chromatography (HPLC) method reported to detect even trace amounts of ascorbic acid in fruit juice or extract (Majeed et al., 2009). Triphala is an anti-oxidant-rich herbal formulation containing fruits of Emblica officinalis, Terminalia chebula and T. Belerica in equal proportions. A developed and validated simple HPLC method for the separation of the major antioxidant polyphenols was also reported (Singh et al., 2008).

The superstation, quantification and free radical-scavenging activity of individual compounds from drug extract were studied based on the combination of HPTLC with a diode array detector and postchromatographic DPPH radical derivatization. Free gallic and ellagic acids and emblicanins A and B in the drug extract were separated by TLC and identified. All the compounds of the extract were capable of scavenging of DPPH radicals (Pozharitskaya et al., 2007).
2.2. Amomum (*Amomum subulatum* Roxb.)

2.2.1. Pharmacological reviews

2.2.1.1. Effect on cardiovascular system and as antioxidant

The antioxidant potential of the amomum was studied along with some of the dietary constituents commonly used in Indian foods to find their effect on the inhibition of lipid peroxidation (LPO) in rat liver homogenate. The reducing power and the superoxide scavenging activity of spice have been also measured *in vitro* and it was observed that activity increased with concentration. Results showed that it significantly reduced LPO due to their polyphenol content with strong reducing power and superoxide radical scavenging activity (Yadav and Bhatnagar, 2007a). A study on the food constituents including amomum was conducted to test their antioxidant properties *in vitro*. It can be concluded that it is a strong antioxidants (Yadav and Bhatnagar, 2007b).

The constituents of the drug were fractionated into three fractions as the dichloromethane extract and the ethyl acetate-soluble and water-soluble fractions of the 70% aqueous acetone extract. The ethyl acetate-soluble fraction showed a high radical-scavenging activity against DPPH. Four compounds were isolated from the ethyl acetate-soluble fraction were characterized as new type of cyclic diarylheptanoid and were showed good antioxidant activity by DPPH method (Kikuzaki *et al*., 2001).

The antioxidant effect of the drug along with cinnamon (*Cinnamomum verum*; Lauraceae) was assessed on hepatic, cardiac antioxidant enzymes, glutathione content and lipid conjugated dienes were studied in rats fed high fat diet along with the drug. The activities were found to be significantly enhanced whereas glutathione content was markedly restored in rats fed a fat diet along with spices. It showed that the drug exert antioxidant protection through their ability to activate the antioxidant enzymes (Dhuley, 1999).

2.2.1.2. Effect on liver

Hepatoprotective effect of the drug was evaluated in CCl₄-induced changes. The drug significantly blocked the CCl₄-induced increase in aspartate aminotransferase and alanine aminotransferase activities. It also showed significant preservation of mitochondrial membrane potential as compared to CCl₄ control demonstrating the
mitochondrial protection. The study suggested that the drug significantly prevented the damage to liver mitochondria through regulation of voltage-dependent anion-selective channel expression (Parmar et al., 2011). The drug was also assessed against ethanol induced hepatotoxicity and it was significantly prevented the functional, physical, biochemical and histological changes induced by ethanol (Parmar et al., 2009).

2.2.1.3. Other studies

The antimicrobial activity of the drug extract was tested against various microorganisms by using disc diffusion method. It revealed that methanol extract of fruits of the drug showed remarkable antimicrobial activity against *Escherichia coli* (Agnihotri and Wakode, 2010).

The drug extract and its different fractions were studied in rats for their ability to inhibit the gastric lesions induced by aspirin, ethanol and pylorus ligature. In addition their effects on wall mucus, output of gastric acid and pepsin concentration were also recorded. The drug extract and its fractions inhibited gastric lesions induced by ethanol. The results suggested that direct protective effect of ethyl acetate fraction on gastric mucosal barrier. The observation of decrease in gastric motility by essential oil and petroleum ether fractions suggested the gastro-protective action of the drug and thus supported the use of 'Heel kalan' in gastrointestinal disorders by Unani physicians (Jafri et al., 2011).

2.2.2. Phytochemistry and analytical reviews

The isolation of cardamonin and alpinetin was carried out from the seeds of amomum. An earlier study on the seeds revealed the presence of a number of terpenes. The constitution of the chalcone was established by hydrolytic cleavage, isomerisation to the corresponding flavanone, UV, IR, NMR data and by comparison with an authentic sample. Powdered ripe seeds of amomum were extracted with ethyl acetate and the oily residue obtained on evaporation of the solvent are separated into a phenolic oil, flavanone and chalcone by chromatography over silica gel using benzene-acetone mixtures for elution. The oil appeared to be a mixture of terpenes and phenols (Bheemasankara et al., 1976).
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2.3. Borage (*Borago officinalis* Linn.)

2.3.1. Pharmacological reviews

2.3.1.1. Effect on cardiovascular system and as antioxidant

The capacity of the aqueous extract of the borage to delay the lipid oxidation process in dry fermented sausages enriched with omega-3 PUFAs has been estimated. It showed antioxidant capacity equivalent to 200ppm of a butylhydroxyanisol and butylhydroxytoluene mixture (Garcia-Iiguez de Ciriano *et al.*, 2009). The hydroalcoholic extract of drug with other edible plants from Calabria region (Italy) showed an anti-inflammatory, radical scavenging and antioxidant properties. The content and the composition of sterols were assessed by GC-MS in the drug which contained the highest number of sterols (Conforti *et al.*, 2008).

The drug has been studied using different isolated tissue preparations including rabbit jejunum, trachea, aorta and guinea-pig atria. In rabbit tracheal preparations, it relaxed the carbachol and 

\[ \text{K}^+ \]

-induced contractions. In rabbit aorta preparations, the drug exhibited vasodilator effect against phenylephrine and 

\[ \text{K}^+ \]

-induced contractions similar to verapamil. These results suggested that the spasmolytic effects of the drug are mediated possibly through \( \text{Ca}^{++} \) antagonist mechanism, which might explain the traditional use of the drug in hyperactive gastrointestinal, respiratory and cardiovascular disorders (Gilani *et al.*, 2007). The rapid assessment of antioxidant activity of crude drug extract was done and determined by using DPPH free radical method along with new HPLC-DPPH on-line method and screened several radical scavenging components in borage extract with quantitative estimation. The dominant antioxidative compound in the crude extract was identified as rosmarinic acid (Bandoniene and Murkovic, 2002).

2.3.1.2. Other activities

The amoebicidal activity was investigated of a methanol extract of the drug. The IC\(_{50}\) of the extract supported the use of borage to prevent diseases associated with *E. histolytica* infection (Leos-Rivas *et al.*, 2011). The borage oil rich in n-6 polyunsaturated fatty acids of which gamma-linolenic acid is rapidly metabolised to longer-chain n-6 polyunsaturated fatty acids, increased T-helper1 like responses and...
decreased T-helper2 like responses and possibly enhanced suppressor cell or T-helper3 like activity (Harbige and Fisher, 2001).

2.3.2. Phytochemistry and analytical reviews

The leaves of the drug were examined in the region of Amdoun (Tunisia) during different stages of their development and essential oil contents varied from 0.01% to 0.13%, respectively in young and adult leaves. Twenty-three volatile compounds were identified. Hydrocarbons, mainly represented by nonadecane, tetracosane and heptacosane, constituted the major class in the young leaves, followed by aldehydes. The percentages of these two classes decreased to reach respectively 15% and 8.1% in adult leaves in favour of alcohols where cis-3-hexenol and hexanol were the main compounds. Total fatty acids amounts increased from 5.03 mg g\(^{-1}\) of dry weight in young leaves to 32.23 mg g\(^{-1}\) of dry weight in adult ones. The predominant fatty acids were alpha-linolenic, stearidonic, gamma-linolenic, palmitic and linoleic acids (Mhamdi et al., 2007).

The separation and identification of rosmarinic acid was achieved by using HPLC-UV-mass spectrometry in 80% methanol in water extracts from the leaves of the drug as well as dominant radical scavenger towards DPPH stable radical in HPLC-DPPH system was also studied. Drug showed good correlation between the rosmarinic acid concentration and antiradical activity (Bandoniene et al., 2005). The glycosylated pyrrolizidine alkaloid, thesinine-4'-O-beta-D-glucoside, has been isolated from the aqueous methanol extract of dried defatted seeds of the drug. The structure was established by means of spectroscopic and chemical analysis (Herrmann et al., 2002) whereas pyrrolizidine alkaloids were also isolated from the drug (Lüthy et al., 1984).
2.4. Cassia (*Cinnamomum cassia* Blume.)

2.4.1. Pharmacological reviews

2.4.1.1. Effect on cardiovascular system and as antioxidant

2-methoxycinnamaldehyde; one of active constituent of *Cinnamomum cassia* Blume reduces vascular cell adhesion molecule-1 expression in tumor necrosis factor-alpha activated endothelial cells and protects ischemia/reperfusion-injury due to heme oxygenase induction. In addition, 2-methoxycinnamaldehyde has been shown to reduce the expression of high mobility group box 1, an activator of the inflammatory cascade and vascular cell adhesion molecule-1 (Hwa *et al*., 2012). Some selected plants along with the cassia evaluated for antioxidant activity to support the hypothesis that formulation of a polyherbal combination of these plants shows a synergistic effect with green tea. The results of the study were suggested that a combination of all these herbs with green tea can synergistically enhance antioxidant activity and thus lower doses of each herb (Jain *et al*., 2011). The antioxidant potential and anticholinesterase activity of the drug were tested by using cupric reducing antioxidant capacity and Ellman methods, respectively. The results indicated that dichloromethane, ethanol and water extracts of the drug showed the good antioxidant effect among the extracts of the tested plants (Boga *et al*., 2011).

The drug extract showed both platelet anti-aggregation and blood anti-coagulation effects in preliminary testing. Among the 13 compounds obtained from this plant, eugenol, amygdalactone, cinnamic alcohol, 2-hydroxycinnamaldehyde, 2-methoxycinnamaldehyde and coniferaldehyde showed 1.5-73-fold greater inhibitory effects than acetylsalicylic acid on arachidonic acid induced aggregation and 6.3-730-fold stronger effect than acetylsalicylic acid on U46619 (a thromboxane A\(_2\) mimic)-induced aggregation. The other compounds, coumarin, cinnamaldehyde, cinnamic acid, icariside DC and dihydrocinnacasside also inhibited U46619-induced aggregation. The eugenol and coniferaldehyde were the two of the most active anti-platelet constituents of the drug (Kim *et al*., 2010).
2.4.1.2. Other activities

The drug extract showed the potent antioxidant activity and cytotoxicity against *Helicobacter pylori* and acid-neutralizing capacity (Jung *et al*., 2011) and showed protective role in liver injury in rats (Lim *et al*., 2010).

Biochemical analysis revealed that the drug showed the anti-diabetic ability by either prevent the decrease in superoxide dismutase activity or suppress the increase of malondialdehyde (He *et al*., 2011). The drug was analysed for cytotoxicity and it induced apoptosis in the cervical cancer cells (Koppikar *et al*., 2010). Cinnamaldehyde and derivatives showed inhibitory effect against human colon cancer cell growth (Lee *et al*., 2007). The drug extract diminished the production of nitric oxide tumor necrosis factor and prostaglandin in lipopolysaccharide activated RAW264.7 cells and it was concluded that the drug exerts strong anti-inflammatory activity (Yu *et al*., 2012). The drug also showed anti-Candida activity (Taguchi *et al*., 2012). Cinnamaldehyde the constituent of cassia was screened against phosphodiesterase-5A1 (PDE5A1) activity. Human recombinant PDE5A1 was used as the enzyme source (Dell Agli *et al*., 2008). It exerted anti-inflammatory effect by blocking the degradation of the inhibitory protein I kappa B-alpha (Liao *et al*., 2008).

2.4.2. Phytochemistry and analytical reviews

Two trimeric proanthocyanidins and cinnamtannins were isolated from the *C. cassia* along with the known tetramer parameritannin and a previously unreported tetramer, named cassiatannin A (Killday *et al*., 2011). A pressurized liquid extraction and GC-MS method was developed for simultaneous quantitative determination of the seven components including cinnamaldehyde, copaene, cinnamic acid, coumarin, 2-methoxycinnamaldehyde, 2-methoxycinnamic acid and safrole in the drug (Lv *et al*., 2010). The twigs extract of the drug was found to possess inhibitory activity against tyrosinase. Purification of the methanol extract afforded four new phenolics together with 10 known compounds, which showed strong inhibitory activity against tyrosinase (Ngoc *et al*., 2009). The GC-MS, chemometric resolution method-Alternative moving window factor analysis that were proposed recently and the Kovats retention index were used to analyze the essential components of cassia. The main pharmacodynamic ingredients cinnamaldehyde was in higher contents (Xiang *et al*., 2008).
2.5. Coriander (*Coriandrum sativum* Linn.)

2.5.1. Pharmacological reviews

2.5.1.1. Effect on cardiovascular system and as antioxidant

The hepatoprotective activity of *C. sativum* studied against CCl<sub>4</sub>-induced toxicity. The drug showed hepatoprotection which may be due to the antioxidant potential of phenolic compounds (Pandey *et al*., 2011). The antioxidant efficacy of hot water extracts of coriander was studied by estimating total phenolic content, total flavonoids content and antioxidant activities. The results indicated that hot water extract of coriander had a high antioxidant activity which is partly due to the phenolic and flavonoid compounds (Kim *et al*., 2011). The production of antioxidants in vegetative parts (leaves and stems) of *in vivo* and *in vitro* grown samples was compared. Seeds were also studied as they are used to obtain *in vivo* and *in vitro* vegetative parts. Lipophilic (tocopherols, carotenoids and chlorophylls) and hydrophilic (sugars, ascorbic acid, phenolics, flavonols and anthocyanins) compounds were quantified. The antioxidant activity was evaluated by radical scavenging activity, reducing power and lipid peroxidation inhibition. The *in vivo* sample showed the highest antioxidant activity mainly due to its highest levels of hydrophilic compounds (Dias *et al*., 2011).

The antioxidant and free-radical-scavenging property of seeds was studied using *in vitro* method and also investigated whether the administration of seeds curtails oxidative stress in the kidney of streptozotocin-induced diabetic rats. Incorporation of seed powder in the diet led to marked lowering of blood glucose as well as increase in the levels of insulin in diabetic rats. The seeds showed scavenging activity against superoxides and hydroxyl radicals in a concentration-dependent manner. The results showed that *C. sativum* seeds not only possess antihyperglycemic properties but antioxidative properties also (Deepa and Anuradha, 2011). The methanolic crude extract of the drug along with other spices were screened for their free radical scavenging properties using ascorbic acid as standard by DPPH method. The present study concluded that the selected plants would exerted several beneficial effects by virtue of their antioxidant activity (Sultana *et al*., 2010). The coriander oil was analyzed by GC-MS and assayed for their *in vitro, in vivo* antioxidant activity and hepatoprotective effect against CCl<sub>4</sub> damage. The *in vitro* antioxidant activity was evaluated as a free radical scavenging capacity, measured as scavenging activity of...
the essential oils on DPPH and hydroxyl radicals and effects on lipid peroxidation in two systems of induction. Some liver biochemical parameters were determined in animals pretreated with essential oils and later intoxicated with CCl₄ to assessed in vivo hepatoprotective effect. The essential oils were able to reduced the stable DPPH in a dose-dependent manner and to neutralize hydrogen peroxide (Samojlik et al., 2010). Antioxidative activities of ethanol extracts from seven Umbelliferae fruits along with coriander have been studied by the DPPH radical scavenging test. All the studied extracts showed antioxidant capability. The extracts were also investigated regarding their total flavonoid contents by the aluminium chloride technique (Nickavar et al., 2009). Coriander extract was evaluated through in vitro and in vivo techniques and it caused atropine sensitive stimulatory effect in isolated guinea-pig ileum. It produced vasodilatation against phenylephrine and potassium induced contractions in rabbit aorta and cardio-depressant effect in guinea-pig atria. It also produced diuresis in rats. The results indicated that coriander fruit exhibits gut stimulatory, inhibitory and hypotensive effects mediating possibly through cholinergic, calcium antagonist and the combination of these mechanisms respectively (Jabeen et al., 2009). The antioxidant activity of coriander was assessed on CCl₄ induced oxidative stress in rats. Pre-treatment of rats with different doses of drug extract significantly lowered SGOT, SGPT and TBARS levels against carbon tetrachloride treated rats. Hepatic enzymes like SOD, CAT and GPx were significantly increased by treatment with plant extract. Oral administration of the leaf extract significantly reduced the toxic effects of CCl₄ the activity was comparable to the standard drug, silymarin (Sreelatha et al., 2009).

Antioxidant properties of essential oils from coriander were studied by capillary gas-liquid chromatography. Antioxidant activity was assessed by oxidation of the aliphatic aldehyde hexanal to the carboxylic acid (Misharina and Samusenko, 2008).

The coriander was studied for its nutritional composition, antioxidant and free radical scavenging activities, it showed lower inhibitory concentration values by DPPH and higher values of anti-radical power method as compared with their seeds. Thermal treatment reduced the total phenolic contents, antioxidant and free radical scavenging activities. The leaves of *C. sativum* were found with good amounts of caffeic acid, ferulic acid, gallic acid and chlorogenic acid (Bajpai et al., 2005). The antioxidant activity of the drug extracts was investigated by comparing with the known...
antioxidant ascorbic acid in *in vitro* studies. The quantity needed for 50% inhibition of hydroxyl radicals 1250 µg of coriander and 4500 µg of ascorbic acid which showed strong antioxidant activity of the drug (Satyanarayana *et al*., 2004). The anti-peroxidative effect of coriander seeds was studied in rats administered high fat diet and significant decrease in the levels of lipid peroxides, free fatty acids and glutathione was observed when compared to control group whereas the activity of antioxidant enzymes showed increase (Chithra and Leelamma, 1999). Hypotensive effect of the drug was also studied in anaesthetized rats with significant results (Medhin *et al*., 1986).

### 2.5.1.2. Effect on CNS

The effect of seed extract has been evaluated on learning in second-generation mice. It can improve learning by long term administration (Zargar-Nattaj *et al*., 2011). The drug also produced anti-anxiety effects (Mahendra *et al*., 2011) and hydro-alcoholic extract, ethyl acetate and n-butanol fraction of the drug significantly prolonged sleep duration whereas n-butanol fraction could significantly decrease sleep latency (Rakhshandeh *et al*., 2011). The drug produced a dose-dependent improvement in memory of young as well as aged mice it may be a useful remedy in the management of Alzheimer's disease on account of its multifarious effects (Mani *et al*., 2011). The aqueous extract of coriander has been studied for anxiolytic effect in mice, which significantly reduced spontaneous activity and neuromuscular coordination compared to control group. The results suggested that the aqueous extract of coriander seed has anxiolytic effect and may have potential sedative and muscle relaxant effects (Emamghoreishi *et al*., 2005).

### 2.5.1.3. Antidiabetic effect

The hypoglycemic and hypolipidemic potential of coriander extract has been demonstrated after a single oral dose for 30 days in normal and obese-hyperglycemic-hyperlipidemic rats. The coriander seed extract decreased several components of the metabolic syndrome, decreased atherosclerotic and increased cardioprotective indices; it may have cardiovascular protective effect. The study validated the traditional use of coriander in diabetes (Aissaoui *et al*., 2011). The ethanol extract of the seeds was investigated for effects on insulin release from the pancreatic beta cells in streptozotocin-induced diabetic rats. The results showed that administration of the
ethanol extract exhibited a significant reduction in serum glucose (Eidi et al., 2009). The coriander incorporated into the diet and drinking water, which reduced hyperglycaemia of streptozotocin-diabetic mice, it increased 2-deoxyglucose transport, glucose oxidation and incorporation of glucose into glycogen of isolated murine abdominal muscle comparable with M-insulin. The results demonstrated the presence of antihyperglycaemic, insulin-releasing and insulin-like activity of the drug (Gray and Flatt, 1999). The effects of the drug on glucose homeostasis were also evaluated in normal and streptozotocin induced diabetic mice. Treatment with coriander reduced the level of hyperglycaemia during the development of streptozotocin diabetes. The results suggested that coriander treatments for diabetes can retard the development of streptozotocin diabetes in mice (Swanston-Flatt et al., 1990).

2.5.1.4. Antimicrobial activity

The antimicrobial activity of the drug was demonstrated using ethyl acetate, acetone and methanol extracts of coriander (Keskin and Toroglu, 2011). The coriander oil showed good antibacterial activity towards the majority of the bacterial strains tested, including *Streptococcus pyogenes* and methicillin resistant *Staphylococcus aureus*. The skin tolerance of a cream and a lotion containing coriander oil was also assessed and no any skin irritation was observed. It was found that coriander oil might be useful as an antiseptic for the prevention and treatment of skin infections with Gram-positive bacteria (Casetti et al., 2012). The comparable quantitative antimicrobial activity of coriander oil was carried out against eleven different bacterial and three fungal strains belonging to species reported to be involved in food poisoning. The coriander oil exhibited considerable good antibacterial capacity against all the organisms tested (Lixandru et al., 2010).

The antimicrobial activity of coriander extract was assessed on multi-drug resistant *Escherichia coli* isolates and it showed anti-bacterial activity against enteric pathogens and could be used for prevention of diarrheal diseases (Rahman et al., 2011). The antibacterial potential of aqueous infusions and aqueous decoctions of coriander was studied against 345 bacterial isolates belonging to 6 different genera of Gram negative bacterial population isolated from urine specimens by employing well diffusion technique (Saeed and Tariq, 2007).
2.5.1.5. Other activities

The coriander played a protective role against the deleterious effects in lipid metabolism in experimental colon cancer (Chithra and Leelamma, 2000) and significantly decreased levels of total cholesterol and triglycerides in animal tissues (Chithra and Leelamma, 1997).

The \textit{in vitro} effect of fractions from coriander has been evaluated on promastigotes and amastigotes of \textit{L. infantum} and to analyze the toxicity against the murine monocytic cells. The methanol fraction of \textit{C. sativum} was found to be most effective against amastigotes and did not differ from the positive control amphotericin B (Rondon \textit{et al.}, 2011). The therapeutic potential of aqueous extract of the drug against metronidazole-induced genotoxicity was examined. The results showed significant increase in both micronucleation and binucleation formation (Talapatra \textit{et al.}, 2010).

The coriander seeds incorporated into diet are shown to possess hypolipidemic action (Dhanapakiam \textit{et al.}, 2008).

The acute diuretic activity of continuous intravenous infusion of aqueous extract of the coriander seed in rats has also been observed. The crude aqueous extract of coriander seeds increased diuresis, excretion of electrolytes and glomerular filtration rate in a dose-dependent way thus, supporting the use of coriander as a diuretic plant in Moroccan Pharmacopoeia (Aissaoui \textit{et al.}, 2008). In the biphasic model of triton-induced hyperlipidemia, the drug reduced cholesterol and triglycerides levels in both synthesis and excretory phases in rats and the results were comparable with that of liponil, a commercially available herbal hypolipidemic drug. The results suggested that coriander decreases the uptake and enhances the breakdown of lipids and may have potential to be herbal remedy with preventive and curative effect against hyperlipidemia (Lal \textit{et al.}, 2004).

2.5.2. Phytochemistry and analytical reviews

The coriander oil was analyzed by GC-MS coupled with chemometric resolution methods. The qualitative analysis was performed by comparing the pure mass spectra with those in the NIST 05 mass spectral library. Quantitative analysis was performed using the total volume integration method. A total of 118 constituents were detected, of which 104 were identified (Zhou \textit{et al.}, 2011). The plant was extracted employing ultrasonication and microwave-assisted extractions and observed that efficiency of
The extraction of bioactive compounds obtained with the microwave extraction process was in general about four times higher than that resulting from sonication extraction (Gallo et al., 2010). The chemical profiles of different accessions of coriander were analysed by means of GC-MS. The essential oil content of the dried seeds varied from 0.1-0.36%. Thirty-four different compounds were identified in the essential oil of all accessions. It was observed that all accessions contained more than 60% linalool showing the high quality of coriander seeds produced in Iran (Nejad Ebralimi et al., 2010).

The HPLC-UV method for the determination of selected antioxidants was developed. Two ultrasonic extraction methods for the isolation of compounds from coriander were used. Both of these methods, i.e. ultrasonic probe and ultrasonic bath, were optimised and compared to each other. For all extracts the antioxidant capacity based on the reduction of free DPPH radical was determined (Adam et al., 2009). The water-soluble portion of the methanol extract of coriander was used to isolate 33 compounds, including two new monoterpenoids, four new monoterpenoid glycosides, two new monoterpenoid glucoside sulfates and two new aromatic compound glycosides and their structures were clarified by spectral investigation (Ishikawa et al., 2003). The drug extract was screened for polyacetylenic compounds using the ELISA for panaxytriol and their antiproliferative activity was checked by MTT assay using the tumour cell lines (Nakano et al., 1998).
2.6. Jatamansi (*Nardostachys jatamansi* DC.)

2.6.1. Pharmacological reviews

2.6.1.1. Effect on cardiovascular system and as antioxidant

The effect of ethanolic extract of jatamansi rhizomes was studied on doxorubicin induced myocardial injury with respect to lipid metabolism in serum and heart of rats. The drug treatment showed a significant prevention in the lipid status with the activities of the lipid metabolizing enzymes in doxorubicin induced rats (Subashini *et al*., 2007). The effect of jatamansi rhizomes on the biochemical changes, tissue peroxidative damage and abnormal antioxidant levels has been estimated in doxorubicin (adriamycin)-induced cardiac damage. The drug significantly prevented these alterations and restored the enzyme activity and lipid peroxides to near normal levels (Subashini *et al*., 2006). The protective effect of jatamansi on neurobehavioral activities, TBARS, reduced glutathione, thiol group, catalase and sodium-potassium ATPase activities has been studied in middle cerebral artery occlusion model of acute cerebral ischemia in rats. All the alternations induced by ischemia were significantly attenuated by jatamansi and correlated well with histopathology by decreasing the neuronal cell death following middle cerebral artery occlusion and reperfusion (Salim *et al*., 2003). The known sesquiterpene valeranone was isolated from the subterranean parts of jatamansi. It was pharmacologically investigated in animal experiments of sedative, tranquilizing and antihypertensive properties. The anti-ulcer action was detected on three other pharmacological models. The valeranone showed weak hypotensive activity (Rücker *et al*., 1978). Antioxidant activity of drug extract was observed, it may be due to high jatamansone content, however further study is needed to study the effect of jatamansone on cardiomyopathy (Tripathi *et al*., 1996).

2.6.1.2. Effect on CNS

Combined pre-treatment with the extract of jatamansi, crocetin and selenium as sodium selenite for 15 days led to improved behavioral outcomes in streptozotocin induced cognitive impairment in rats. The study reflected the synergistic potential of the above combination and concluded that a multimodal approach could be beneficial rather than a singular intervention (Khan *et al*., 2011). The neuropsychopharmacological effect of a polyherbal formulation containing jatamansi as one of the ingredients was determined on the learning and memory processes in
rats. The formulation produces significant improvement in passive avoidance acquisition and memory retrieval in rats (Shah and Goyal, 2011). The antidepressant and anti-stress effect of jatamansi was evaluated on experimental rat model of chronic fatigue syndrome. There was a significant increase in despair behaviour and anxiety in stressed control animals on successive days of chronic fatigue syndrome. Administration of jatamansi tended to normalize augmented lipid peroxidation, nitrite, superoxide dismutase activities and catalase level significantly (Lyle et al., 2009a). The anti-stress effect of jatamansi extract was evaluated in reference to its antioxidant property in rats. The assessment of stress-induced alterations in biochemical parameters, incidence and severity of ulcers showed potent antioxidant activity as well as reversed the stress-induced elevation of LPO and NO levels and decrease in catalase activity in the brain (Lyle et al., 2009b).

The drug extract produced significant antidepressant-like effect in both tail suspension and forced swim tests in mice. The results showed that the antidepressant-like effect of the extract may also be due to interaction with GABA-B receptors (Dhingra and Goyal, 2008). The hydroalcoholic extracts of six herbs including jatamansi used in Indian systems of medicine were tested for \textit{in vitro} acetylcholinesterase inhibitory activity which showed that the hydro alcohol extract of jatamansi inhibited half of acetyl cholinesterase activity (Mukherjee et al., 2007). It was also investigated \textit{in vitro} and observed that methanolic extract to be more active than water extract. The potent acetyl cholinesterase inhibiting effect of methanolic extract of jatamansi was observed (Vinutha et al., 2007). The drug significantly improved learning and memory in young mice and also reversed the amnesia induced by diazepam and scopolamine as well as reversed aging-induced amnesia due to natural aging of mice (Joshi and Parle, 2006). The ethanolic extract of jatamansi roots, an antioxidant and enhancer of biogenic amines can slow the neuronal injury in a rat model. The results exhibited by an increased density of tyrosine hydroxylase immunoreactive fibers in the ipsilateral striatum of the lesioned rats by the drug (Ahmad et al., 2006). The extract was also assessed for its anticonvulsant activity and neurotoxicity, alone and in combination with phenytoin in rats. The results demonstrated a significant increase in the seizure threshold by jatamansi root extract against maximal electroshock seizure model as indicated by a decrease in the extension/flexion ratio (Rao et al., 2005).
2.6.1.3. Other studies

The drug extract showed hepatoprotective activity against thioacetamide induced hepatotoxicity in rats. It significantly ameliorated the liver damage and increase in the level of GABA and taurine when compared to the controls (Prabhu et al., 1994) and

The diabetogenic effect of streptozotocin was completely abolished when mice were pre-treated with jatamansi extract. The drug also significantly reduced cytokine-induced NF-kappaB activation and downstream events, inducible nitric oxide synthase expression and nitric oxide production. The drug extract provided resistance to pancreatic beta-cell damage from cytokine or streptozotocin treatment (Song et al., 2010). The drug treatment attenuated acute pancreatitis by reducing edema, neutrophil infiltration, serum amylase, lipase levels, serum cytokine levels and messenger RNA expressions of inflammatory mediators against cerulein-induced acute pancreatitis (Bae et al., 2010). It also inhibited lipopolysaccharide-induced endotoxin shock and the production of inflammatory mediators (Bae et al., 2011).

The aqueous extract of jatamansi showed antioxidant and anticataleptic effect in the haloperidol-induced catalepsy rat model (Rasheed et al., 2010). The drug was also screened for antimicrobial properties and found that the crude extracts of jatamansi exhibited significant antimicrobial activity (Kumar et al., 2006).

2.6.2. Phytochemistry and analytical reviews

The isolation of terpenoid compounds nardal, jatamansic acid and nardin were carried out from the extract of jatamansi by fractionation. These compounds were identified based on physical and spectral data and comparison with authentic compounds (Gottumukkala et al., 2011). A rapid and highly sensitive UPLC-QTOF MS method was developed and analysis was carried out and developed method was validated for the linearity, accuracy and precision (Mallavadhani et al., 2011). The structure and stereochemistry of a new terpenoid ester, nardostachysin, isolated from the drug was established (Chatterjee et al., 2000). Two new eudesmanes jatamols A and B were isolated from the roots and rhizomes of jatamansi (Bagchi et al., 1991a). The dichloromethane extract of jatamansi was analysed by 13C-NMR and 1H-NMR. One new neolignan was isolated and identified with 2 known neolignans and 2 lignans (Bagchi et al., 1991b).
2.7. Saffron (*Crocus sativus* Linn.)

2.7.1. Pharmacological reviews

2.7.1.1. Effect on cardiovascular system and as antioxidant

Saffron has been systematically evaluated for cardioprotection in isoproterenol-induced myocardial damage in rats and it was observed that, it exerted significant cardioprotective effect by preserving hemodynamics and left ventricular functions, maintaining structural integrity and augmenting antioxidant status (Sachdeva *et al.*, 2010). Saffron showed remarkably decreased intensity of tissue destruction and significantly decreased serum level of heart troponin I, when compared to isoproterenol group. It showed the protective role of saffron on ischemic hearts (Joukar *et al.*, 2010). The saffron extract, safranal and crocin reduced the mean arterial blood pressure in normotensive and hypertensive anaesthetized rats in a dose-dependent manner (Imenshahidi *et al.*, 2010). The antioxidant activity along with estimation of phenolic and flavonoid compounds of saffron was assessed using different extracts. The saffron showed antioxidant activity by free radical scavenging and ferric reducing power method. The higher activity was found in the methanolic extract of saffron as compared to the corresponding boiling water and ethanolic extracts (Karimi *et al.*, 2010).

The effect of crocin, a pharmacologically active constituent of saffron was evaluated in isoproterenol-induced cardiotoxicity with reference to hemodynamic, antioxidant, histopathological and ultrastructural parameters. The preventive role of crocin on isoproterenol-induced myocardial infarction was reconfirmed by histopathological and ultrastructural examinations. It was observed that crocin may have cardioprotective effect in isoproterenol-induced cardiac toxicity through modulation of oxidative stress (Goyal *et al.*, 2010). The hypolipidemic and antioxidant potential of saffron and its active constituent, crocin were studied in hyperlipidemic rats. Biochemical estimations in liver tissue homogenate were carried out and observed that the both saffron and crocin were effective in decreasing the elevated levels of TG, TC, ALP, AST, ALT, MDA, GSHPx, GSH and GSSG in serum and increasing SOD, CAT, FRAP and SH values in liver tissue with reduction in TBARS. The saffron was found to be superior to crocin indicating the involvement of other potential constituents of saffron apart from crocin for its synergistic behavior of quenching the
free radicals and ameliorating the damages of hyperlipidemia (Asdaq and Inamdar, 2010). It was determined whether crocetin has beneficial effects on cardiac injury caused by hemorrhagic shock and resuscitation in rats. The results suggested that crocetin blocks inflammatory cascades by inhibiting reactive oxygen species production and preserving superoxide dismutase activity to ameliorate the cardiac injury caused by hemorrhage/resuscitation (Yan et al., 2010). A study also showed that the drug may have potential as antioxidant and antimicrobial agent (Sengul et al., 2009). The drug and its constituents were observed to decrease ischemia-reperfusion injury in kidney or brain tissues and it was concluded that saffron extract and its constituent showed a protective effect against lower limb ischemia-reperfusion in rat (Hosseinzadeh et al., 2009). The effects of crocetin on platelet activity and thrombosis formation were systematically investigated. It showed a dose-dependent inhibition of platelet aggregation induced by ADP, collagen, but not by arachidonic acid. It was concluded that the favorable impacts of crocetin on platelet activity and thrombosis formation may be related to the inhibition of Ca$^{2+}$ elevation in stimulated platelets (Yang et al., 2008). The effects of an aqueous-ethanol extract of drug on heart rate and contractility were determined and observed a potent inhibitory effect of aqueous-ethanol extract of saffron on the calcium channel of guinea-pig heart (Boskabady et al., 2008). The effect of crocin on ischemia/reperfusion injury was assessed in mice cerebral microvessels. The crocin markedly inhibited oxidizing reactions and modulated the ultrastructure of cortical microvascular endothelial cells in mice with 20 min of bilateral common carotid artery occlusion followed by reperfusion in vivo. The crocin protected the brain against excessive oxidative stress (Zheng et al., 2007). The mechanism of the curative action of drug extract was studied by doing a number of experiments on Chinchilla rabbits with experimental models of retinal dystrophy. The results indicated the antioxidative function plays a crucial role in the curative action of saffron extract and serves as a pathogenetic basis for its application in visual impairments of various origins (Shukurova and Babaev, 2010).

2.7.1.2. Effect on CNS

The protective effect of saffron extract and honey syrup was assessed on neurotoxicity induced by aluminum chloride in mice. Biochemical and molecular studies concluded that the neurotoxicity of aluminum chloride in the brains of mice was ameliorated with saffron extract and honey syrup (Shati et al., 2010).
A study was suggested that crocin and crocetin provide neuroprotection by reducing the production of various neurotoxic molecules from activated microglia (Nam et al., 2010). In a study, to assess the efficacy of saffron in the treatment of mild to moderate Alzheimer's disease on forty-six patients, saffron produced a significantly better outcome on cognitive function than placebo without significant differences in the two groups in terms of observed adverse events (Akhondzadeh et al., 2010). Crocin could significantly attenuate learning and memory impairment against streptozocin toxicity in passive avoidance test model (Khalili and Hamzeh, 2010). Saffron was found to be effective similar to donepezil in the treatment of mild-to-moderate Alzheimer's disease. The study provided preliminary evidence of a possible therapeutic effect of saffron extract in the treatment of patients with mild-to-moderate Alzheimer's disease (Akhondzadeh et al., 2010). The effects of aqueous and ethanolic extracts of saffron and its constituents were determined on morphine-withdrawal syndrome in mice. Dependence was induced using subcutaneous injections of morphine for three days. It was concluded that the extracts and crocin may have interaction with the opioid system to reduce withdrawal syndrome (Hosseinzadeh and Jahanian, 2010).

The aqueous ethanol extract of stigmas and corms of saffron was evaluated for antidepressant properties as well as fractionated on the basis of polarity. The petroleum ether fraction and dichloromethane fraction showed significant antidepressant-like activities in dose-dependent manners by means of behavioural models of depression. Saffron corms extract produced antidepressant-like effects and aqueous stigmas extract also exerted antidepressive effects in the behavioural models. Crocin 1 and crocin 2 of the aqueous stigmas extract were identified by a reversed-phase HPLC analysis. In addition, the bioactive compound crocin 1 in this herb was quantitatively determined (Wang et al., 2010). The neuroprotective effect of drug extract and its active component crocin and gamma-glutamylcysteinylglycine was assessed in glucose-induced neurotoxicity using PC12 cells as a suitable in vitro model of diabetic neuropathy. It was suggested that saffron and its carotenoid crocin may be potentially useful in diabetic neuropathy treatment (Mousavi et al., 2010). The anxiolytic and hypnotic effects of aqueous extract of saffron and its constituents, crocin and safranal were studied in mice. The aqueous extract reduced the locomotor activity dose dependently and observed that saffron aqueous extract and safranal have anxiolytic and hypnotic effects (Hosseinzadeh and Noraei, 2009). It was also studied...
in the rat that treatment with active constituents of saffron induced anxiolytic-like effects in the rat (Pitsikas et al., 2008). The effect of crocins was studied on recognition and spatial memory in rat. The results supported and extend the enhancing effects of crocins on memory (Pitsikas et al., 2007). The effect of saffron was study to confirm whether neuroprotective property caused solely by crocin and examined the antioxidant and GSH-synthetic activities of these crocins in PC12 cells under serum-free and hypoxic conditions. Measurements of cell viability, peroxidized membrane lipids and caspase-3 activity showed neuroprotection as crocin>tricrocin>dicrocin and picrocrocin. The carotenoid, significantly reduce infarcted areas caused by occlusion of the middle cerebral artery in mice (Ochiai et al., 2007).

2.7.1.3. Anticancer effect

Saffron decreased the cell viability in the malignant cells as a concentration- and time-dependent manner and induced apoptosis of the A549 cells (Samarghandian et al., 2011). The potential of the ethanolic extract of saffron was studied to induce anti-proliferative and cytotoxic effects in cultured carcinomic human alveolar basal epithelial cells in comparison with non-malignant (L929) cells. The results showed that the ethanolic extract of saffron decreased cell viability in malignant cells as a concentration and time-dependent manner (Samarghandian et al., 2010). A crocin-mediated growth inhibition and apoptotic cell death was elucidated in a human pancreatic cancer cell line (BxPC-3). It exhibited apoptotic morphology and reduction of volume (Bakshi et al., 2010).

The in vitro and in vivo xenograft growth inhibition by crocin isolated from Kashmiri saffron was assessed and found that crocin decreased cell viability in DLA cells in a concentration and time-dependent manner (Bakshi et al., 2009) and saffron inhibited the formation of skin papillomas in animals as well as reduced their size (Das et al., 2010). The drug also showed significant growth inhibitory effects on the growth of TCC 5637 and normal L929 cell lines (Feizzadeh et al., 2008). It can decrease cell viability in malignant cells as a concentration and time-dependent manner (Tavakkol-Afshari et al., 2008). The anti-proliferative effects of saffron extract and its major constituent, crocin was studied on three colorectal cancer cell lines by MTS assay. Significant concentration-related inhibition effects of the extract on all three colorectal cancer cell lines were observed (Aung et al., 2007). Promising and
selective anti-cancer effects of saffron have been observed in vitro and in vivo (Schmidt et al., 2007).

### 2.7.1.4. Other activities

Saffron has been shown to reduce the gentamicin-induced increases in BUN, serum creatinine, MDA and histological injury dose dependently (Ajami et al., 2010). The saffron also minimized biochemical and molecular hepatotoxicity induced by aluminium chloride (Shati and Alamri, 2010).

Crocin, a unique carotenoid with a short carbon chain length is an active compound of saffron investigated for its pharmacokinetic profile in healthy adult subjects. Plasma concentrations of crocin were determined by HPLC. Crocin was rapidly absorbed and detected within an hour of administration with a mean time to reach maximum concentration (Umigai et al., 2011). The effect of crocin and safranal was studied against sub-acute toxicity of diazinon on hematological and genotoxicity indices in rats using the micronucleus assay. Vitamin E at lower doses, safranal and crocin restored the reduction of red blood cells, hemoglobin and hematocrit indices induced by diazinon (Hariri et al., 2011). The effects of crocin were studied in vitro on retinal damage by tunicamycin or hydrogen peroxide exposure. The results indicated that crocin has protective effects against retinal damage in vitro and in vivo (Yamauchi et al., 2011). The effect of safranal on histamine receptors was observed on two groups of tracheal chains incubated with indomethacin and indomethacin with propranolol and atropine (Boskabady et al., 2011). Saffron as an antioxidant is positively effective on sperm morphology and motility in infertile men but its does not increase sperm count (Heidary et al., 2008). The relaxant effects of saffron extracts with one of its constituent safranal were also observed on beta-adrenoceptors in tracheal chains of guinea pigs (Nemati et al., 2008).

### 2.7.2. Phytochemistry and analytical reviews

Total crocin was extracted from saffron using crystallization method and ethanol 80% was found as the best extraction solvent. Crocin crystals obtained from the first crystallization had low purity and thus were subjected to the second crystallization. The higher purity crystals were yielded in the second crystallization at 5.0°C. The purity of crocin crystals was studied using UV-visible spectrophotometry and HPLC (Hadizadeh et al., 2010).
The crocetin esters content was determined by liquid chromatography in saffron. The results showed that the proposed methodology gives data with acceptable accuracy (Anastasaki et al., 2010). Volatile components of saffron from different regions of Iran have been extracted by ultrasonic-assisted solvent extraction and were analyzed by GC-MS. A selective and sensitive HPTLC method was developed and validated for the quantitative analysis of safranal in saffron extract and in nano formulation. The method was found to be accurate and was selective for safranal (Pathan et al., 2010). The simultaneous determination of 46 semi-volatile organic contaminants and pollutants in saffron was estimated by developing a method using a stir bar sorptive extraction technique and thermal desorption in combination with gas chromatography-ion trap tandem mass spectrometry (Maggi et al., 2008). The effect of centrifugal ultrafiltration on the composition of aqueous extract of saffron spice has been assessed. The contents of seven crocetin esters, picrocrocin and two kaempferol glycosides were analyzed by UV-vis and HPLC in the filtrate and retentate fractions from 16 centrifugal filter devices with regenerated cellulose and polyethersulfone membranes. The device showed a potential to obtain picrocrocin without crocetin esters and could be considered in successive ultrafiltration steps (Sánchez et al., 2008).

The HPLC methods have been developed and validated for quality control including the quantification of crocins one to five, crocetin, picrocrocin and the degradation products. The GC-MS method has allowed to detect and quantify volatile compounds in the pentane extract of saffron. Both systems together allowed the comprehensive characterisation of saffron herbal material and extracts for clinical/preclinical trials (Lechtenberg et al., 2008). The phytochemical changes were studied in saffron aroma on storage by collecting six samples from different areas of Italy by analyzed by solid-phase microextraction-GC-MS. Safranal is the main component in all of the samples but long term storage can change its yield (Dauria et al., 2006).

The artificial colours in saffron were estimated by removal of crocins by precipitation of crocetin before adsorption of the artificial colours on polyamide SPE cartridges. The lowest detectable amount for each colour was strongly dependent on chemical structure and this method can replace the current ISO TLC method and can be used alternatively or in combination with HPLC procedures adopted in the same standard (Zalacain et al., 2005). Crocetin has been found to enhanced the oxygen diffusivity.
through liquids such as plasma and increased alveolar oxygen transport and enhanced
pulmonary oxygenation improved cerebral oxygenation in hemorrhaged rats as well as positively acted in the atherosclerosis and arthritis treatment. It inhibits skin tumor
promotion in mice; it has an inhibitory effect on intracellular nucleic acid and protein
synthesis in malignant cells as well as on protein-kinase-C and prorooncogene in
INNIH/3T3 cells. The valuable effects are most likely due to its anti-oxidant activity.
It also has a protective effect on the bladder toxicity induced by cyclophosphamamide
(Giaccio, 2004). Safranal is the main component of saffron's essential oil obtained
using micro simultaneous hydro distillation-extraction and by ultrasound-assisted
extraction. 4-Hydroxy-2, 6, 6-trimethyl-1-cyclohexene-1-carboxaldehyde is a
precursor of safranal and it was obtained in considerable amounts only by ultrasound-
assisted extraction. Five norisoprenoids were found in saffron for the first time. The
safranal and its precursor were quantified by gas chromatography technique from
Greek saffron samples (Kanakis et al., 2004). The Changes in aroma and colouring
properties of saffron after gamma-irradiation were investigated using GC-MS by
isolating volatile essential oil. HPLC Analysis revealed a decrease in glucosides and
an increase in aglycon content in irradiated samples it showed the possible
degradation of pigments during gamma irradiation (Zareena et al., 2001). A
supercritical carbon dioxide extraction method for volatile compounds of saffron
without sample destruction has been developed. Supercritical extracts from five
different saffron types were studied by HPLC and their safranal contents were
determined (Lozano et al., 2000). The saffron components in crude plant extracts was
estimated by HPLC-UV-visible photodiode-array detection on-line with mass
spectrometry. The determination of picrocrocin, the glycosidic precursor of safranal
and flavonoids was carried out (Tarantilis et al., 1995).
2.8. Sandal \((Santalum album \text{ Linn.})\)

2.8.1. Pharmacological reviews

2.8.1.1. Anticancer effect

The chemopreventive effects of sandalwood oil was demonstrated on 7, 12-dimethylbenz(a)anthracene-(DMBA)-initiated, 12-O-tetradecanoyl phorbol-13-acetate(TPA)-promoted skin papillomas and TPA-induced ornithine decarboxylase (ODC) activity in CD1 mice were studied. It significantly decreased papilloma incidence, multiplicity and TPA-induced ODC activity (Dwivedi and Abu-Ghazaleh, 1997). The effect of sandal oil on glutathione S-transferase activity and acid soluble sulphhydryl levels in the liver of mice was studied. It was observed that it increased in acid-soluble SH levels in the hepatic tissue of the mice and it suggested that a possible chemopreventive action of sandalwood oil on carcinogenesis through a blocking mechanism (Banerjee et al., 1993).

2.8.1.2. Antimicrobial effect

The sandal oil has been observed to have anticarcinogenic, antiviral and bactericidal activity (Burdock and Carabin, 2008). Sandal has been shown to be effective in reducing lipid oxidation and microbial counts in raw sheep meat (Luo et al., 2007). Six new sesquiterpenes isolated from sandal along with the crude extracts showed antibacterial activity against \(H. \text{ Pylori}\) (Ochi et al., 2005). The sandal oil was studied for in vitro antiviral activity against \(Herpes simplex\) viruses-1 and -2. It was observed that the replication of these viruses was inhibited by the oil dose-dependently (Benencia and Courrèges, 1999).

2.8.1.3. Other activity

The antihyperglycemic and antihyperlipidemic effect of petroleum ether fraction of sandal was studied in streptozotocin-induced diabetic rats. Drug demonstrated reduction in blood glucose level and anti-hyperlipidemic activity (Kulkarni et al., 2011). A dose-dependent NO scavenging activity was observed with sandal suggesting that the drug may be potent and novel therapeutic agents for scavenging of NO and the regulation of pathological conditions caused by excessive generation of NO (Jagetia and Baliga, 2004).
The effects of East Indian sandal oil and alpha-santalol were investigated on physiological parameters as well as on mental and emotional conditions in healthy human subjects after trans-dermal absorption. It was observed that alpha-santalol caused significant physiological changes which are interpreted in terms of a relaxing/sedative effect; sandalwood oil provoked physiological deactivation but behavioral activation (Burdock and Carabin, 2008).

2.8.2. Phytochemistry and analytical reviews

A new neolignan, (7R, 8R)-5-O-demethylbilagrewin and four known lignans were isolated from the heartwood of sandal (Matsuo and Mimaki, 2010). The extraction of secondary metabolites was designed for sandal plant cell suspensions using bench-top bioreactor. There was no any essential oils were detected as secondary metabolites in the form of phenolics were produced by the sandalwood cell cultures (Valluri, 2009). Six new bisabolane-type and santalane-type sesquiterpenoids with (+)-alpha-nuciferol, (+)-citronellol and geraniol were isolated from the heartwood of sandal of Indian origin (Kim et al., 2005a). The polar constituents were also investigated in the heartwood of Indian sandal and resulted in the isolation of three new neolignans and a new aromatic ester (Kim et al., 2005b). Trade and historic oils from sandalwoods were assessed using GC-MS. It was observed that none of the oils assessed complied with the internationally recognised standard of 90% santalol content (Howes et al., 2004).