Chapter-8

8. SUMMARY AND CONCLUSION

Plant materials are used throughout the developed and developing world as home remedies, in over-the-counter drug products, and as raw material for the pharmaceutical industry, and they represent a substantial proportion of the global drug market. Certain herbs have become popular over the years, but the public, medical practitioners and the media still have a poor understanding of herbal medicine. Evidence is emerging on the dangers of herbs. As in most situations, the truth lies hidden under the media hype, poorly understood science, and exaggerated claims. Lack of experience, information, and education about herbs make consumers, physicians, and other orthodox health care provider’s easy victims of market exploitation and herbal myths. There is no rational reason behind the tendency to equate “natural” with “harmlessness.”

The fact that something is natural does not necessarily make it safe or effective. In addition, a lack of knowledge of phytochemistry leads to misinterpretation and misunderstanding. It is very likely that some herbs will have side effects, interact with other medications, and be toxic. Information on isolated constituents should not be applied directly to the whole herb and studies on in vitro forms should not be confused with oral administration was established by pharmacological screenings.

In current scenario, herbs are the potent sources of medicines used in the treatment of various disease and disorders. Since, plants are used as medicine there is prompt need of evaluation of plant species, therefore, the present work was conceived to evaluate the phytochemical and pharmacological screening of few Indian medicinal plants.
The Pharmacognostical evaluation of Indian medicinal plants viz., leaves of *Gymnema sylvestre*, fruits of *Momordica charantia*, rhizomes of *Curcuma longa*, seeds of *Eugenia jambolana* and fruits of *Embilica officinalis* were studied which include the morphological, anatomical and physicochemical studies. The morphological and anatomical studies of species plant part were studied which will be beneficial for the validation and assessment of quality control parameters of these plants to find out the presence of adulterant if any in order to establish the quality, safety and efficacy.

From the data of physicochemical analysis it was concluded that these plants has optimum level of carbon content which was establish by the ash content data. The moisture content was found to be maximum in EJS followed by EOF, MCF, CLR and GSL. The swelling index was found to be maximum in EJS i.e, 4.28. The FOM was found maximum in EOF. The extractive values results indicate that alcohol soluble extractive value, soluble extractive value and ether soluble extractive value were recorded and being presented in Chapter. The percentage yield value of various extracts was estimated and results indicate that EEMCF was found maximum i.e., 15.39% w/w whereas EEJS was found maximum i.e, 6.45% w/w.

From the results of preliminary phytochemical screening it was concluded that the ethanolic extracts contained various phytochemicals such as alkaloids, glycosides, saponins, carbohydrates etc.

Pre-formulation parameters such as bulk density, tap density, Carr's index, Hausner's ratio and angle of repose were studied and investigated for the granules. The polyherbal formulation (capsule and vati) were formulated and evaluated as per standard protocols. The detailed results were mentioned in Chapter. From the
results obtained it was revealed that the Formulation code F5 for both herbal capsule and vati were optimized formulation. Further, the optimized formulations F5 were study for stability. Stability studies at three different temperatures and RH as per ICH guidelines i.e., $25^\circ C \pm 2^\circ C/ 60\% \pm 5\%$ RH (SS-I), $30^\circ C \pm 2^\circ C/ 65\% \pm 5\%$ RH (SS-I) and $40^\circ C \pm 2^\circ C/ 75\%$ (SS-III) were studied for formulated herbal capsule and vati and it was found from the data that both the formulation at SS-II were giving promising results as compared to two other i.e., SS-I and SS-III.

In the present study various standardization parameters such as physicochemical standards like loss on drying, disintegration test, weight variation test, dissolution test, hardness test and friability were carried out. It can be concluded that the formulation has been standardized by intervention of modern quality control measures. Pharmacognostic characters established for the raw materials could be employed as quality control standards for evaluating its identity and can be used for routine analysis. The tablets have been evaluated on the basis of the above mentioned parameter which shows satisfactory results. The study shows that the contents of formulation presents within the permissible limits as per WHO. All these investigations parameter are specified in the standard literature such as in pharmaocopoeia, which could helpful in authentication of vati. Ingredients of this formulation were useful in the treatment of diabetes and hyperlipidemic conditions.

Free radical oxidative stress has been implicated in the pathogenesis of variety of diseases, resulting usually from defective natural antioxidants, hence therapy should include either enzymes or natural antioxidant enzymes, which are capable of augmenting the function of these oxidative free radical scavenging enzymes. By virtue of their proposed properties and clinical use in Ayurveda, polyherbal formulations may provide potential, therapeutic intervention against oxidative threats, both in health and diseased conditions. Phytoconstituents such as flavonoids,
terpenoids, alkaloids, glycosides present in the polyherbal formulation, act as natural free radical scavengers.

The results of antioxidant activity suggest that polyherbal formulation possesses significant antioxidant activity as compared with standard drug. The results of reducing power shows an increase in absorbance of the polyherbal formulation in a dose related manner which indicates the increased reducing power of the extract.

Thus the ethanolic extracts of polyherbal formulation possess good reducing power and antioxidant activity.

*In vitro* dissolution has been recognized as an important element in drug development under certain assessment of Bioequivalence. Several theories/kinetics models describe drug dissolution from immediate and modified release dosage forms. The drug release kinetics were studied for both the optimized formulation i.e., herbal capsule and vati, formulation code F5. From the results it was concluded that the above formulation possess Korsmeyer-Peppas model.

Acute toxicity profile were studied and recorded for both the optimized formulation. Since no any mortality were observed at the dose of 2000 mg/kg, therefore the LD$_{50}$ is 2000 and 1/10$^{th}$ is ED$_{50}$ i.e., 200 and one upper dose of 400 was selected.

Alloxan induced diabetic model was given in two dose levels,(200 and 400 mg/kg b.w). At the dose level of 200 mg/kg b.w serum glucose level showed a significant decrease.During the course of 10 study alloxan induced diabetes mellitus, blood glucose levels were estimated on day 1, day 4, day 7 and day 10. Day 1 was compared with day 10.In diabetes control group, the changes were non-significant.

In group treated with standard antidiabetic drug, Glibenclamide, the decrease in blood glucose was significant on day 4, day 7, and on day 10. Rats treated with 200mg/kg b.w. of Capsule and Vati showed significant decrease after day 7 and day 10.The Capsule formulation showed more significant effect.
During the course of 10 days alloxan induced diabetes mellitus average body weight was recorded on day 1, day 4, day 7 and day 10. Day 1 was compared with day 10. Diabetic control rats showed significant decrease in body weight from day 1 to day 10. Glibenclamide (standard antidiabetic drug) produced significant decrease in body weight on day 10. Both formulation at the dose of 200 & 400 mg/kg b.w showed significant increase in body weight.

Results of anti-diabetic activity of formulation extracts established the scientific basis for the utility of these plants in the treatment of diabetes. The formulated herbal capsule and vati at the dose of 200 and 400 mg/kg BW have shown significant reduction in blood glucose levels in both glucose loaded and STZ-NIC induced diabetic rats. The herbal capsule produced maximum anti-diabetic activity and is higher than the hypoglycemic activity of glibenclamide in the diabetic rats. Therefore it is obvious that the fractionation with herbal capsule has enriched the active principles. In glucose loaded animals, the drug has reduced the blood glucose to the normal levels. It is possible that the drug may be acting by potentiating the pancreatic secretion or increasing the glucose uptake. Both herbal capsule and vati has reduced the glucose levels, in prolonged treatment study. Histopathological examination of liver and pancreas showed the recovery of damaged tissues when section of treated groups compared with diabetic control.

In conclusion, these formulations showed significant anti-diabetic effect in diabetic rats after oral administration. Thus the claim made by the traditional Indian systems of medicine regarding the use of these plants in the treatment of diabetes stands confirms.

STZ is toxic glycoside obtained from *Streptomyces achromogenes*, a gram-positive bacterium. It accumulates in pancreatic β cells via the glucose transporter 2 (GLUT2) and reduces their expression. The alkylating properties of the STZ modify the biological macromolecules, fragment DNA, and destroy the β cells, causing insulin-dependent diabetes. In the diabetic control group, severe body weight loss
was observed, which may be due to increased muscle wasting and loss of tissue proteins. In the present study, the treatment groups showed significant improvement in body weight, which indicates that polyherbal formulation and glibenclamide prevent the hyperglycemia-induced muscle wastage. The reduction in glucose levels may be due to increase in plasma insulin levels or enhanced transport of blood glucose in the peripheral tissue. The study gives evidence that the polyherbal formulation increases the plasma insulin levels and has promising antidiabetic activity. Diabetic animals showed enhanced levels of HbA1c due to excessive production of glucose in blood, which further reacts with blood hemoglobin and produces HbA1c.

The diabetic hyperglycemia induced by STZ and NIC causes elevation of plasma levels of SGPT, SGOT, urea, and creatinine, which are considered as significant markers of liver and renal dysfunction. The polyherbal formulation treated animals reversed the effect of STZ and NIC on the liver and renal markers. This may be due to the hepatoprotective mechanism of the individual herbs present in the polyherbal formulation.

STZ diabetic rat has increased levels of lipid peroxides and reactive oxygen species, which cause hyperglycemia. Incessant generation of free radicals can lead to tissue damage through peroxidation of unsaturated fatty acids. The polyherbal formulation treated animals inhibited the hyperglycemia induced by STZ, which may be due to the free radical scavenging properties of the individual herbs present in it.

Histopathology of the pancreas of STZ diabetic animals showed severe decrease in the number of islets of Langerhans and β cells, with fibrosis and inflammatory cell infiltration into the islets of Langerhans, and these findings are supported by the
reports published earlier. Histopathology of the liver of STZ diabetic animals showed a severe fatty change, sinusoidal dilation and congestion, mild portal inflammation, fibrosis, severe feathery degeneration, and necrosis. The hepatic changes may be due to the hypertrophy of hepatocytes by an increase in the intracytoplasmic eosinophilic granules. Polyherbal formulation and glibenclamide treatment to the animals reduced the severity of the histopathologic changes caused by STZ.

Thus, the study findings demonstrate the antidiabetic effect of the polyherbal formulation at the dose levels of 200 and 400 mg/kg. The antidiabetic potential of the polyherbal formulation is comparable with that of glibenclamide, which is evidenced by decreased levels of blood glucose, HbA$_{1c}$, total cholesterol, triglyceride, low density lipoprotein (LDL)-cholesterol, urea, creatinine, SGOT, and SGPT, and increase in plasma insulin, HDL-cholesterol, liver glycogen, and total protein levels.

Hence, from the present work it was concluded that the selected medicinal plants of Indian origin possess optimum activity which will claims their folk-lore uses as mentioned in traditional system of medicine.