CHAPTER IV

4. LITERATURE REVIEW

4.1. LITERATURE REVIEW ON ANTIDIABETIC EFFECT OF MEDICINAL PLANTS IN HIGH FAT DIET INDUCED DIABETES MODEL

Numerous types of diabetic models were used for screening antidiabetic properties of plants. These diabetic models are developed using several methods either through genetic or chemically induced diabetes (Zhang X et al., 2012). Genetic models of diabetes known as db/db mouse and Zucker diabetic fatty (ZDF) rats which develop similar features as in human type 2 diabetes. These rats are expensive to be used as diabetic models for pharmacological screening (Masiello P et al., 2006). Meanwhile, development of diabetic rats following streptozotocin (STZ) injection also produce hyperglycemia. However, this method only develops insulin deficiency rather than insulin resistance in the model. Despite that, the pattern of disease progress did not appear to be similar to diabetic situation in human type 2 diabetes mellitus. Recently, many studies reported that rats induced with high fat diet have developed similar situation as type 2 diabetes progress in humans. Diets containing high fat will cause insulin resistance in peripheral tissues due to lipotoxicity. It has been shown that high-fat-fed animal can weigh more than chow-fed controls within a week of starting the high-fat diet (Winzell Ms et al., 2004), although typically animals are fed the high-fat diet for several weeks to induce a more pronounced weight gain. The weight gain is associated with insulin resistance and lack of beta cell compensation leads to impaired glucose tolerance.

The approach of feeding HF diet for the induction of T2D was first described during late 1980s (Surwit RS, 1988). Obesity is one of the major factors for the
development of T2D and it usually develops when rodents are fed a diet containing high amounts of fat (40–60% of the total calories). Several researchers have developed this model by using C57BL/6J mice. The high-fat diet models are usually characterized by overweight, obesity, impaired glucose tolerance and insulin resistance. The C57BL/6J mice are typically fed a diet containing 40–60% of calories from fat, approximately eight times higher fat content than that of control mice for 8–16 weeks. Although some of the diabetic features were noted just after 4 weeks; however, the longer duration of fat-feeding enhances the features of insulin resistance, impaired glucose tolerance revealing elevated serum insulin and glucose, abnormal lipid profile and mild to moderate hyperglycemia. However, the major disadvantage of this model is the duration of time (>10 weeks) required to induce the all major pathogenesis of T2D particularly hyperglycemia and insulin resistance, which is not suitable for many researchers, as this increases the cost of the experiment.

High-fat diet–fed mouse is a robust and efficient model for early type 2 diabetes and may therefore be used for both mechanistic studies and as a tool for developing novel therapeutic interventions. Previous literatures revealed that antidiabetic effect of various herbal extracts and herbal formulations were successfully screened by this method. Some of them were listed in table 4.1
### Table 4.1: Antidiabetic Effect of Herbal Drugs in High Fat Diet induced Diabetes Model

<table>
<thead>
<tr>
<th>Herbal drug</th>
<th>Animals</th>
<th>Induction method</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Curculigo latifolia</em></td>
<td>Male Sprague dawley rats</td>
<td>HFD for 4 weeks + 40mg/kg STZ</td>
<td>Akmal <em>et al.</em>, 2013</td>
</tr>
<tr>
<td><em>Hylocereus undatus</em></td>
<td>Male C57BL/6J mice</td>
<td>HFD for 14 weeks</td>
<td>Haizha <em>et al.</em>, 2016</td>
</tr>
<tr>
<td><em>Fenugreek seed</em></td>
<td>Male C57BL/6 mice</td>
<td>HFD for 12 weeks</td>
<td>Kandhare <em>et al.</em>, 2015</td>
</tr>
<tr>
<td><em>Holostemma annularis</em></td>
<td>Male Wistar albino rats</td>
<td>High Fructose Diet for 3 weeks</td>
<td>Reddy <em>et al.</em>, 2010</td>
</tr>
<tr>
<td><em>Brown seaweeds</em></td>
<td>Male C57BL/6N mice</td>
<td>HFD for 16 weeks</td>
<td>Ji Hyum <em>et al.</em>, 2016</td>
</tr>
<tr>
<td><em>Centaurium erythraea</em></td>
<td>Male C57BL/6J mice</td>
<td>HFD for 17 weeks</td>
<td>Nawel hamza <em>et al.</em>, 2011</td>
</tr>
<tr>
<td>Herbal formulation contains 8 herbal components</td>
<td>Male C57BL/6J mice</td>
<td>HFD for 6 weeks</td>
<td>Yushu Huoet al <em>et al.</em>, 2013</td>
</tr>
<tr>
<td><em>Trigonella foenum graecum</em></td>
<td>Male C57BL/6J mice</td>
<td>HFD for 17 weeks</td>
<td>Nawel hamza <em>et al.</em>, 2013</td>
</tr>
<tr>
<td><em>Xylia dolabriformis</em></td>
<td>Male C57BL/6J mice</td>
<td>HFD for 3 weeks</td>
<td>Amaranth 2013</td>
</tr>
<tr>
<td><em>Bougainuillea spectabilis</em></td>
<td>Male albino rats</td>
<td>HFD for 8 weeks</td>
<td>Saikiaet <em>et al.</em>, 2011</td>
</tr>
<tr>
<td><em>Silybrun marianum</em></td>
<td>Male Sprague Dawley rats</td>
<td>HFD for 11 weeks</td>
<td>Fatima <em>et al.</em>, 2016</td>
</tr>
<tr>
<td><em>Artemisia capillaries</em></td>
<td>Male wistar rats</td>
<td>HFD for 8 weeks</td>
<td>Dong wook <em>et al.</em>, 2013</td>
</tr>
<tr>
<td><em>Rhizoma polygonati odorati</em></td>
<td>Male C57BL/6J mice</td>
<td>HFD for 12 weeks</td>
<td>Gu M <em>et al.</em>, 2013</td>
</tr>
<tr>
<td><em>Cichorium intybus</em></td>
<td>Male albino wistar rats</td>
<td>HFD for 4 weeks + 30mg/kg STZ</td>
<td>Emam A <em>et al.</em>, 2016</td>
</tr>
<tr>
<td><em>Phlorizin</em></td>
<td>Male C57BL/6J mice</td>
<td>HFD for 16 weeks</td>
<td>Su Kyung <em>et al.</em>, 2016</td>
</tr>
</tbody>
</table>
4.2. LITERATURE REVIEW ON INFLUENCE OF NANOTECHNOLOGY ON HERBAL DRUGS

Pharmacological properties of herbal formulation mainly depend on overall functions of a variety of phytochemical constituents present therein. These phytochemical components, generally referred to as secondary metabolites, include terpenoids, phenolics, steroids and alkaloids. Each of the active constituents plays a vital role and all are related to each other. Some of these phytochemical constituents possess insoluble character leading to lower bioavailability and increased systemic clearance and requiring repeated administration or higher dose, which makes the drug as a poor candidate for therapeutic use (Yogita et al., 2015). Also most of the active constituents of the herbal drugs will be destroyed in the highly acidic pH of the stomach before reaching to the blood and other constituents might be metabolized by the liver. Resulting, the optimum quantity of the herbal drugs may not reach the blood. If the drug does not reach to the infected region at effective level, then there will be no therapeutic effect of the drug. These limitations of plant origin drugs can be overcome by attaching or encapsulating them with suitable nanomaterials. Nanotechnology combined with herbal science is the recent technique used to overcome the limitations of using herbal drugs. Nanocarriers applying to herbal remedies will carry optimum amount of the drug to their site of action bypassing all the barriers such as acidic pH of stomach, liver metabolism and increase the prolonged circulation of the drug into the blood due to their small size (Kumari et al., 2012). Table 4.2 explains the herbal medicine incorporated nanoparticles and its applications.
# 4.2. Herbal Medicine Incorporated Nanoparticles and its Applications

<table>
<thead>
<tr>
<th>Herbal Drug</th>
<th>Polymer used</th>
<th>Method</th>
<th>Particle size (nm)</th>
<th>Therapeutic effect</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrabidaea chica</td>
<td>Chitosan</td>
<td>Ionic gelation</td>
<td>150</td>
<td>Antiulcer</td>
<td>Leila Servat et al., 2015</td>
</tr>
<tr>
<td>Rubus coreanus</td>
<td>Gelatin</td>
<td>Ultrasonication</td>
<td>143</td>
<td>Immunomodulatory</td>
<td>Yong Chang et al., 2011</td>
</tr>
<tr>
<td>Phyllanthus amarus</td>
<td>Poly vinyl alcohol</td>
<td>Nanoprecipitation</td>
<td>243</td>
<td>Hepatoprotective</td>
<td>Shanti Bhushan et al., 2013</td>
</tr>
<tr>
<td>Gelsemium sempervirens</td>
<td>PLGA</td>
<td>Solvent displacement</td>
<td>122.6</td>
<td>Anticancer</td>
<td>Sowmya Sundar et al., 2010</td>
</tr>
<tr>
<td>Polygala senega</td>
<td>PLGA</td>
<td>Solvent displacement</td>
<td>147.7</td>
<td>Anticancer</td>
<td>Saini Paul et al., 2011</td>
</tr>
<tr>
<td>Abutilon indicum</td>
<td>Stearic acid, soya lecithin</td>
<td>Ultrasonic homogenization</td>
<td>169</td>
<td>Antimicrobial activity</td>
<td>Rajesh et al., 2014</td>
</tr>
<tr>
<td>Emblica officinalis</td>
<td>Polyvinyl pyrrolidine</td>
<td>Solvent evaporation</td>
<td>550</td>
<td>Anti oxidant and Anti inflammatory</td>
<td>Renuka et al., 2013</td>
</tr>
<tr>
<td>Ziziphus mauritiana</td>
<td>Chitosan</td>
<td>Ionic gelation</td>
<td>395</td>
<td>Immunomodulatory</td>
<td>Aruna Bhatia et al., 2011</td>
</tr>
<tr>
<td>Cissus quadrangularis</td>
<td>Polyvinyl pyrrolidine</td>
<td>Solvent evaporation</td>
<td>155.4</td>
<td>Anti oxidant and Anti inflammatory</td>
<td>Subhashri et al., 2014</td>
</tr>
<tr>
<td>Tridax procumbens</td>
<td>polyvinyl pyrrolidine</td>
<td>Solvent evaporation</td>
<td>200</td>
<td>Antioxidant, Anticancer and Anti inflammatory</td>
<td>Remya Devi et al., 2014</td>
</tr>
<tr>
<td>Berberine</td>
<td>Polyethylene glycol</td>
<td>High pressure homogenization</td>
<td>294.6</td>
<td>Antidiabetic</td>
<td>Zhiping Wang et al., 2015</td>
</tr>
<tr>
<td>Catharanthus roseus</td>
<td>Chitosan</td>
<td>Ionic gelation</td>
<td>283</td>
<td>Antidiabetic</td>
<td>Abul Barkat et al., 2013</td>
</tr>
<tr>
<td>Plant Name</td>
<td>Carrier Material</td>
<td>Method</td>
<td>Molecular Weight</td>
<td>Application</td>
<td>Reference</td>
</tr>
<tr>
<td>--------------------------</td>
<td>------------------</td>
<td>---------------------------------</td>
<td>-------------------</td>
<td>----------------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td><em>Talinum portulacifolium</em></td>
<td>Lipids</td>
<td>Ultrasonication homogenization</td>
<td>260</td>
<td>Antidiabetic</td>
<td>Hima bindu et al., 2014</td>
</tr>
<tr>
<td><em>Enicostemma littorale</em></td>
<td>Alginate</td>
<td>Emulsion coacervation</td>
<td>233</td>
<td>Antidiabetic</td>
<td>Saleha et al., 2016</td>
</tr>
<tr>
<td><em>Balanites sp</em></td>
<td>PLGA</td>
<td>Nanoprecipitation</td>
<td>175</td>
<td>Antidiabetic</td>
<td>Deepa et al., 2012</td>
</tr>
<tr>
<td><em>Stevia rebaudiana</em></td>
<td>Chitosan</td>
<td>Ionic gelation</td>
<td>176</td>
<td>Antidiabetic</td>
<td>Venkatachalam et al., 2016</td>
</tr>
<tr>
<td>Rebaudioside A</td>
<td>PLA</td>
<td>Nanoprecipitation</td>
<td>175</td>
<td>Antidiabetic</td>
<td>Indu barwel et al, 2014</td>
</tr>
<tr>
<td>Baicalin</td>
<td>Miglyol, precirol</td>
<td>High pressure homogenization</td>
<td>92</td>
<td>Antidiabetic</td>
<td>Feng shi et al, 2016</td>
</tr>
<tr>
<td><em>Casia fistula</em></td>
<td>Gelatin</td>
<td>Emulsification</td>
<td>328</td>
<td>Anticancer</td>
<td>Zeinab et al., 2015</td>
</tr>
<tr>
<td><em>Costus speciosus</em></td>
<td>PLGA</td>
<td>Solvent displacement</td>
<td>156</td>
<td>Antidiabetic</td>
<td>Ebtihal et al., 2014</td>
</tr>
<tr>
<td><em>Phyllanthus emblica</em></td>
<td>PLGA</td>
<td>Solvent displacement</td>
<td>176</td>
<td>Antidiabetic</td>
<td>Nadahassan et al., 2016</td>
</tr>
<tr>
<td><em>Phyllanthus amarus</em></td>
<td>Sodium alginate</td>
<td>Emulsification</td>
<td>213</td>
<td>Hepatoprotective</td>
<td>Deepa et al., 2012</td>
</tr>
<tr>
<td><em>Fenugreek seed</em></td>
<td>PLGA</td>
<td>Solvent evaporation</td>
<td>187</td>
<td>Antidiabetic</td>
<td>Walvekar et al., 2016</td>
</tr>
<tr>
<td><em>Garcinia mangostana</em></td>
<td>Eudragit R100</td>
<td>Nanoprecipitation</td>
<td>70</td>
<td>Anticancer</td>
<td>Abdalrahim et al., 2015</td>
</tr>
<tr>
<td><em>Aerva lanata</em></td>
<td>Chitosan</td>
<td>Ionic gelation</td>
<td>250</td>
<td>Anti urolithiatic</td>
<td>Uthaya chandirika et al., 2015</td>
</tr>
<tr>
<td><em>Achyranthus aspera,</em></td>
<td>Chitosan</td>
<td>Emulsion</td>
<td>172</td>
<td>Antimicrobial</td>
<td>Chandrasekar et al., 2013</td>
</tr>
<tr>
<td><em>Syzygium jambolanum</em></td>
<td>PLGA</td>
<td>Solvent evaporation</td>
<td>122</td>
<td>Antidiabetic</td>
<td>Asmita samaddar et al., 2012</td>
</tr>
</tbody>
</table>
4.3. PLANTS PROFILE

4.3. *Myxopyrum serratum* A.W.Hill

Name of the plant : *Myxopyrum serratum*

Family : Oleaceae

Synonyms : ---

4.3.1. Vernacular Names

Hindi : Pilacameli

Malayalam : Caturamulla, caturavalli

Sanskrit : Hemamalati

Tamil : Caturamullai

Telungu : Caturdharalata

4.3.2. Geographical Distribution

Throughout Kerala in evergreen forests at attitudes of 600 to 900 m

4.3.3. Morphology

A large scandent shrub with 4-angled branches; leaves simple, opposite, obovate, elliptic, serrulate, triplicostate; flowers small, yellowish in axillary or terminal trichotomous panicles, stamens 2, attached to the base of the corolla tube; fruits obovoid berries with one or two seeds; seeds erect, testa membranous (Warrier *et al.*, 1994) (Figure 4.1).

4.3.4. Taxonomy

Kingdom : Plantae

Phylum : Magnoliophyta

Class : Magnoliopsida

Order : Lamiales
### 4.3.5. Ethanomedical information

The roots are useful in scabies and prurigo in children; the leaves are astringent acrid, sweet, thermogenic, anodyne, febrifuge and tonic. They are useful in vitiated conditions of kapha and vata, cough, asthma, rheumatism, cephalagia, nostalgia, consumption, fever, otopathy, neuropathy, cuts and wounds (C.P Khare 2008)

The leaves are powdered and taken with ghee as remedy for asthma, cough, rheumatism, nervous complaints and consumption. Leaves were boiled in oil and applied for fever, headache, ear diseases and backaches.

**Figure 4.1: Photograph of Myxopyrum serratum A.W.Hill and its Flower part**
4.3.6. Pharmacological and biological information

Gopalakrishnan S et al., in 2012 reported the antibacterial and antifungal activities of petroleum ether (40-60°C), benzene, chloroform, ethanol and water extracts of the leaves of *Myxopyrum serratulum* A. W. Hill. in Agar diffusion assay. Among all the extracts tested; the ethanolic extract showed a good antimicrobial potential.

Gopalakrishnan S et al., in 2012 reported the pharmacognostical and phytochemical studies *Myxopyrum serratulum*. The results of the pharmacognostical and phytochemical studies can be used as a diagnostic tool for the correct identification of the plant.

Gopalakrishnan S et al., in 2013 studied the GC-MS analysis ethanolic extract of *Myxopyrum serratulum*. Five chemical constituents have been identified.

Sheela Rani T et al., in 2013 evaluated the quantification of phytoconstituents in methanolic extract of *Myxopyrum serratulum* A.W Hill in order to determine the content of phenol, tannin, alkaloid and flavonoid in the crude extract.

Sheela Rani T et al., in 2013 evaluated the in vitro antioxidant activity of methanol extract of *Myxopyrum serratulum* A.W Hill using DPPH and Nitric oxide scavenging activity with reference to standard drug (ascorbic acid). It indicates that the medicinal plant is a better source of antioxidant which might be helpful to prevent the progress of oxidative stress.

Gopalakrishnan S and Rajameena Rajangam R in 2013 evaluated the wound healing activity of the ethanol extract of the leaves of *Myxopyrum serratulum* A.W. Hill in rats. The results showed that significant increase in the wound contraction on the extract treated animals in excision wound model.
Sheelarani T et al., in 2015 studied the levels of heavy metal and trace element in *Myxopyrum serratum* A.W Hill. The concentration of trace elements like Copper, Zinc, Iron is found to within prescribed limit as per WHO Guidelines.

Rajalakshmi K and Mohan V R in 2016 evaluated anti-inflammatory activity of ethanol extracts of stem and leaf of *Myxopyrum serratum* by carrageenan induced rat paw edema model in rats. The study results suggested that *M. serratum* stem and leaf extracts possess strong anti-inflammatory property.

Sheelarani T et al., in 2014 carried out the *in vitro* antiarthritic and anti-inflammatory activity in aerial parts of *Myxopyrum Serratulum* A.W Hill using protein denaturation method and HRBC membrane stabilization method respectively. *In vitro* study results brings out the fact that the ethanolic extract possess better activity compared to the standard drug diclofenac sodium.

Vijayalakshmi M and Ruckmani K in 2016 investigated the presence of various secondary metabolites in the methanolic extract of *M. serratum* by thin layer chromatography and quantified the secondary metabolites by gravimetric analysis. Phytochemical investigation indicated that the presence of flavonoids, phenols and higher concentration of tannin and saponins.
4.4. *Nilgirianthus ciliatus* Nees

Name of the plant : *Nilgirianthus ciliatus*

Family : Acanthaceae

Synonyms : *Strobilanthes ciliatus*

4.4.1. Vernacular Names

Hindi : Karvi, Kara

Malayalam : Karimkurunni, Kurunni, Vellakurunni

Sanskrit : Shacarah, Sairyakah

Tamil : Kurunji, Sinnakurungi

4.4.2. Geographical Distribution

Throughout the evergreen forests of western chats up to 1,200 m. Kanara to Travancore.

4.4.3. Morphology

A small shrub; stems and branches terete or sub quadrangular often fimbriate at the nodes. Leaves 10-18 by 2.5-5 cm, lanceolate, acuminate, lineolate (densely so above), glabrous or nearly so, serrate, base attenuated in to the petiole; main leaves 6-7 pairs; petioles 1.3-3.8 cm long sometimes obscure. Flowers in auxiliary slender glabrous. Spikes 2.5-7.5 cm long; peduncles long, slender, glabrous jointed and bracteates below the middle and deflexed; bracts 6 mm long, ovate, sub-acute, glabrous, lineolate, the margins often obscurely toothed; bracteoles 4 mm long shorter than the calyx, linear, mucronulate, lineolate, glabrous. Calyx 6 mm, long, glabrous or nearly so; tube about 1.25 mm long; segments sub equal, linear, sub obtuse (Figure 4.2). Corolla white, 13-16 mm long; tube narrow in the lower part, campanulate swollen in the upper half; lobes 3 mm long oblong, rounded at the
apex, spotted with lilac at the base. Stamens 4, exerted; filaments of the longer stamens bearded; anthers purple; ovary glabrous; style glabrous capsules not seen (Warrier PK et al., 1994)

4.4.4. Taxonomy

<table>
<thead>
<tr>
<th>Kingdom</th>
<th>Plantae</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phylum</td>
<td>Tracheophyta</td>
</tr>
<tr>
<td>Class</td>
<td>Dicotyledons</td>
</tr>
<tr>
<td>Order</td>
<td>Lamiales</td>
</tr>
<tr>
<td>Family</td>
<td>Acanthaceae</td>
</tr>
<tr>
<td>Genus</td>
<td>Nilgirianthus</td>
</tr>
<tr>
<td>Species</td>
<td>Nilgirianthus ciliatus</td>
</tr>
<tr>
<td>Botanical name</td>
<td>Nilgirianthus ciliatus</td>
</tr>
</tbody>
</table>

4.4.5. Ethanomedical information

*Nilgirianthus ciliatus* is highly potential medicinal plant in Ayurveda and widely used in different medicinal preparations like Sahacharadi thailam, Sahacharadi kashayam, Varanadi kashayam, Bhonagathailam, Ashtavargam kashayam, Maharasnadi kashayam, Sathavaryadi kashayam, Balasahcharadi kashayam, Balaaireyakadi kashayam, Balakulathhadi kashayam, Balala shunakandadi kashayam and Aragwadharishtam.

The roots are bitter, sweet, thermogenic, emollient, diuretic, febrifuge, diaphoretic, depurative, anti-inflammatory, expectorant and tonic. They are useful in rheumatalgia, lumbago, sciatica, limping, chest congestion, strangury, fever, leucoderma, skin diseases, inflammations, cough, bronchitis, odontalgia and general debility (Kiritikar KR & Basu BD) The leaves and bark are diaphoretic, expectorant, depurative and febrifuge and are useful in whooping cough, fever, bronchitis,
dropsy, leucoderma, leprosy, inflammation, scrofula and fever. Leaves are applied externally in gout, lumbago and pain in joints, used in the treatment of jaundice, dropsy, rheumatism and disease of urinogenital tract. The extract of leaves and bark is suggested for itching, leprosy, diabetes, tooth ache and urinal disorders. In folk medicine the drinking of the leaf decoction and applying of leaf paste over affected area for relieving rheumatic pain has been practiced. Kurinji kuzhambu is another medicinal preparation given for ladies after delivery for good health (Khare C.P 2008).

Figure 4.2: Photograph of *Nilgirianthus ciliatus* Nees and its flower part

![Photograph of Nilgirianthus ciliatus Nees and its flower part](image)

4.4.6. Pharmacological and biological information

Venkatachalapathi S *et al.*, in 2012 isolated one compound from *Strobilanthes ciliatus*. Lupeol was isolated from the petroleum ether extract of aerial parts of *Strobilanthes ciliatus Nees* by column chromatography and identified by IR, NMR and MS spectral data. It was quantified in the petroleum ether extract by HPTLC method and found to be 0.16±0.02% w/w.
Chapter IV

Lupeol

Reneela P et al., in 2010 evaluated the phytochemical investigation on the stems of *Strobilanthes ciliatus* Nees. The separation of the chemical components was carried out by chromatography and structures of the compounds were elucidated by spectroscopic methods. The compounds were identified as Lupeol, Stigmasterol, Betulin, and Stigmasterol glycoside.

Stigmasterol  
Betulin  
Stigmasterol glycoside

Reneela P et al., in 2011 isolated one new compound from *Strobilanthes ciliatus*. Chemical constituents of *Strobilanthes ciliatus* were investigated by means of chromatographic techniques. A new compound 4-Acetyl-2, 7-dihydroxy-1, 4, 8-triphenyl-octane-3, 5-dione was isolated and elucidated on the basis of spectral data.

Nataraja Thamizh Selvam et al., in 2013 evaluated the Hepatoprotective activity of *Nilgirianthus ciliatus* (Nees) bremek by paracetamol induced toxicity in Wistar albino rats. The study showed the methanolic extract of *N. ciliatus* having significant hepatoprotective effect as evidenced by the decreased liver marker enzyme levels when compared with the control.
Sudharsan Nair et al., in 2013 described the phytochemical constituents and antioxidant activities of ethanol leaf extract of *Nilgirianthus ciliatus* and its protective effect against H₂O₂-induced DNA damages in cultured lymphocytes. The ethanol extract exhibited a significant dose dependent inhibition in *in vitro* radical scavenging assays. The DNA protection was observed at 60 μg/ml of *Nilgirianthus ciliatus* against 500 μM H₂O₂ treated lymphocytes.

Jayaraman S et al., in 2014 evaluated the phytochemical and biological properties of the plant of *Strobilanthes ciliatus* Nees. Analgesic property of the plant extract was evaluated against the standard drug Pentazocin using tail clip models. The extract of *Strobilanthes ciliatus* Nees showed more significant analgesic activity as compared to standard drug.

Annie Shirwaikar et al., in 2015 determined the anti-diabetic activity of *Strobilanthes ciliatus* in streptozotocin-nicotinamide induced diabetic rats. The alcoholic extract showed significant reduction in blood sugar level when compared with normal rats (p<0.05) and their effect was equivalent to that of reference drug Glibenclamide.

Neethu Varghese et al., in 2014 identified the phytochemical constituents and also evaluated the antibacterial and antifungal activity of *Nilgirianthus ciliatus* on four bacterial pathogens and two fungal strains. The extracts showed significant antimicrobial activity and were compared with Amoxicillin and Ketoconazole.

Brahma Srinivasa Rao Desu et al., in 2015 studied the anti-inflammatory activity of ethanolic extract of *Strobilanthes ciliatus* aerial parts using carrageenan induced paw oedema model in wistar rats. The test extract showed significant anti-inflammatory activity when compared to standard drug diclofenac and vehicle control.
Asha Thomas and S. Rajeshkumar in 2014 conducted a pot culture investigation to know the influence of inoculation with the fungus *Glomus aggregatum* and the plant growth promoting *Rhizomicroorganisms, Trichoderma harzianum* and *Bacillus coagulans* singly and in combination on productivity of *Strobilanthes ciliatus*. The maximum root colonization and spore number were also observed in plants inoculated with *Glomus aggregatum + Bacillus coagulans + Trichoderma harzianum*.

4.5. LITERATURE REVIEW ON POLYMER

4.5.1. GELATIN PROFILE

Over the past few decades, ongoing research interest has been conceded to gelatin based drug delivery systems (Young *et al.*, 2005) for several reasons. The underlying rationale is due to their exceptional properties i.e. non-antigenicity, biodegradability, biocompatibility, chemical modification potential, extraordinary loading capacity, controllable drug release as well as good storage stability. The overall beneficial properties of gelatin is classified as GRAS (generally regarded as safe) material by the U.S. Food and Drug Administration (FDA) and has been safely used in foods, cosmetics and pharmaceutical products for a long time (Elzoghby A.O *et al.*, 2012). The natural source of gelatin is from animals. It is obtained mainly by acidic or alkaline but also thermal or enzymatic degradation of the collagen. Commercially, two types of gelatin are available, gelatin type A, prepared by acidic hydrolysis of porcine skin type I collagen, with an isoelectric point of 6-9, can be distinguished from type B (basic) and gelatin type B, prepared by alkaline hydrolysis of bovine collagen, with an isoelectric point of 4.8-5.0. Gelatin is not a single chemical entity, but a mixture of fractions composed entirely of amino acids joined by peptide linkages to form polymers varying in molecular mass from 15,000 to 400,000.
Gelatin, in terms of basic elements is composed of 50.5% carbon, 6.8% hydrogen, 17% nitrogen and 25.2% oxygen. It contains specific amounts of 18 different amino acids (AA) which are joined together in sequences to form polypeptide chains. 1000 AA per chain, scientifically known as the primary structure (Figure 4.3). The amino acid composition of gelatin is dominated by approximately 33% glycine which orients into the core of the triple-helix and a further 24% proline and 4-hydroxyproline. The rest are other residues. Gly-X-Y represents the continuously repeating amino acid sequence (Figure 4.4). A typical structure is “Ala-Gly-Pro-Arg-Gly-Glu-4Hyp-Gly-Pro”.

Figure 4.3: Structure of gelatin

Being a versatile natural polymer, gelatin has a broad range of applications i.e. food, photographic, medical and pharmaceutical products. In the medical field it is used in artificial organs and tissue engineering. In pharmaceutical field it is conventionally used as emulsifier, binder, gelling agent, vaccine stabilizer and plasma expander. Due to its innate properties it has gained new interests in drug delivery systems such as hydrogels, films, microcapsules, nanoparticles, etc.
4.5.2. APPLICATIONS OF GELATIN NANOPARTICLES

Gelatin nanoparticles (GNPs) are very efficient in drug delivery and controlled release of the drugs, proteins and peptides. GNPs based delivery system is biocompatible and biodegradable without toxic degradation products in body. Several methods have been used to synthesize GNPs, including desolvation, coacervation and water-in-oil (w/o) emulsion, solvent worse or precipitation. Gelatin nanoparticles are better stable in biological fluids to provide the desired controlled and sustained release of entrapped drug molecules. It has also given emphasis on the major applications of gelatin nanoparticles in drug and vaccine delivery, gene delivery to target tissues and nutraceutical delivery for improving the poor bioavailability of bioactive phytonutrients. Cellular uptake of these nanoparticles is mainly attributed to endocytosis, wherein the cells engulf the nanoparticles, forming a vesicular structure (endosome) that fuses with the lysosomes within the cytoplasmic space. Upon acidification of the endo-lysosomal complex, the nanoparticles degrade and the contents are released into the cytoplasm to exert pharmacological action. GNPs have
been extensively investigated for the delivery of anti-cancer drugs, e.g. methotrexate, cytarabine, resveratrol and cisplatin. The preferable feature of GNPs for anti-cancer drug delivery concerns the passive targeting ability due to the enhanced permeability and retention effects, through which GNPs can remain at the tumor target for a long time to achieve the complete release of loaded drugs. Insulin (Zhao Y Z et al., 2012), bovine serum albumin (BSA), alkaline phosphatase (ALP) and angiogenic basic fibroblast growth factor (Magadala P et al., 2008) have been successfully encapsulated into GNPs with retained \textit{in vivo} bioactivity. GNPs have been under investigation for various administration routes including per oral, ocular, pulmonary and parenteral. Furthermore, because of these advantages, the technology of nano-encapsulation has been extended to natural products over the past decade to protect them from chemical damage and product degradation, especially from air oxidation and therefore extent the product’s shelf-life before its final application.
4.6. REFERENCES


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