CHAPTER I

Pharmacognosstkal, Phytochemical and Pharmacological studies on
Dalbergia species - A review

1.1 Introduction

Natural products from plants, animals and minerals have been serving as sources of drugs for the treatment of human diseases since time immemorial. Our ancestors derived therapeutic materials from thousands of plants. Considerable research on pharmacognosy, phytochemistry, pharmacology, toxicology and to a lesser extent, on clinical pharmacology is being carried out on medicinal plants\(^7\). Of late, many of the major pharmaceutical industries have renewed their interest in favour of plant drugs. Numerous drugs have entered international pharmacopoeia through the study of ethnopharmacology and traditional remedies.

Naturally occurring medicines are of great importance as a reservoir of chemical diversity aimed at new drug discovery and are screened for many pharmacological studies like antimicrobial, antihypertensive, immunomodulatory, anti-inflammatory, antioxidant, antidiabetic, anticancer activities etc. Around 80% of all such products are of plant origin\(^2\). Herbal medicines are becoming very popular, not only in developing countries with a long tradition in the use of medicinal plants but also in some developed countries like Germany, France, Italy and the United States\(^3,4\). The future discovery of naturally occurring drugs depends mainly on the wise use of ancient and modern therapeutic skills in a complementary manner so that the community may be provided with maximum benefits\(^5\). Lag phase for plant medicines is now changing rapidly. Problems with drug resistant micro-organisms, adverse effects of
modern drugs, emerging diseases for which no proper medicines are currently available etc., have stimulated our renewed interest in plants as a significant source of new medicines. Pharmaceutical scientists are experiencing a lot of difficulty in identifying new lead structures and templates in the vast world of chemical diversity. As synthetic drugs have been known to have adverse and unwanted side effects, emphasis is being made in the development of potent, safe and novel drugs from natural sources. The recent success in the field of plant based drugs is most notably from Chinese medicines.

A whole range of chronic diseases such as cancer, hypertension, diabetes, rheumatism, immunodeficiency syndrome etc. require novel drugs and most of the developing countries rely and will continue to rely on traditional medicines since the drugs of modern system of medicine are not only costly and urban oriented and hence not available to the common man but also possess a variety of side effects. Recent studies indicate that about 80% of people in developing countries still rely on traditional medicines, based largely on various species of plants. According to the WHO, because of poor economic conditions and also lack of access to modern system of medicines, about 65-80% of the world’s population in developing countries depend essentially on plants for their primary health care. It is reported that four out of every ten Americans used alternative medicine therapies in 1997 and the number of total visits made by Americans to practitioners of alternative medicine has increased by almost 50% from 1990 till date.

1.2 Herbal drug development

Looking towards the arena of medicinal plant drugs, herbal drug development needs to include various steps, starting from collection of
data on raw materials, pharmacognostic and phytochemical quality standardization, experimental and clinical pharmacology and randomized, controlled clinical trials. Lately, many international bodies, including the WHO, US Agency for Health Care Policy and Research and the Dept, of Indian System of Medicine have started creating new regulations to include and regulate quality control and standardization of medicines of plant sources. Currently existing regulatory methods for herbal medicines include drug prescription, over-the-counter drugs, traditional medicines and dietary supplements and hence the need for establishment of global and/or regional regulatory mechanisms for regulating herbal drugs seems obvious.

A basic requirement for preparation of a herbal drug of good pharmaceutical quality involves the use of optimum quality and quantity of the herbal drug. Its constituents significantly influence the quality of the herbal drug and thus the efficacy and safety of the resulting herbal medicinal products. For this reason, both the quality and reproduction of the total spectrum of constituents of the herbal drug are extremely important. However, since the herbal drugs are always composed of a complex mixture of different chemical constituents, it is not possible to define all of them and to determine them during quality control.

According to the current state of scientific knowledge, only those constituents that are relevant to ensure efficacy and safety are used to characterize the quality of the drugs.

Standardization of drugs is a very important aspect of the manufacture and the supply of herbal drugs. It is only in recent years, the importance of standardization of herbal products is realized and efforts are being made to satisfy the regulatory requirements. Many of the
manufacturers export herbal extracts without proper standardization and the importers also accept them since it is very expensive to check the purity by modern methods of standardisation at their end. However this cannot go on for long and regulations are likely to be applied strictly to herbal products in all developed nations, though it may not be possible to apply the parameters of quality control and standardization to herbal drugs as applicable to modern synthetic drugs. At present, it has been widely accepted that characterization of active constituents is mandatory for the standardization of herbal medicines, whether they are in the extract form or in the pure isolate form.

Recent advances in chemical and biological techniques have resulted in many scientific evidences to substantiate the use of herbal products enabling the manufacturers to produce standardized herbal medicinal products. Although there is an ever growing demand of indigenous plants for their medicinal use all over the world, particularly in the developing countries, the world continues to lose its plant species through deforestation, urbanization etc. The knowledge based on the use of indigenous medicinal plants as therapeutic agents is constantly getting eroded due to vanishing of informations and improper documentation of ancient systems of medicines. Therefore scientists have to take efforts not only to catalogue the actual uses of medicinal plant species, develop research programmes in this field, not only to assess the utility of plants in the light of modern scientific informations but also to apply suited measures to isolate and identify the active principles.

Use of active constituents, enriched by solvent extraction instead of powdered plant materials, will result in value addition, enhancement in the efficacy of products and the manufacture of value-added products.
Isolation and characterization of active ingredients, wherever possible, will lead to value addition by 250-500 percent depending on the nature of the products. In addition to the drugs of plant origin, dry extracts, soft extracts, infusions, tinctures, volatile oils etc., containing partially purified secondary active principles are also being widely used to fight against diseases.

The isolates which are homogenous and pure are generally employed, only if active principles of extracts show strong and specific activities with a small therapeutic index and hence require an accurate dosage. Currently, the chemical entities extracted from various species of higher plants in the near pure form, are being used in the field of medicine throughout the world\textsuperscript{17}.

Progress achieved over the last four decades in natural products isolation has been made possible, partly due to the tremendous development of separation techniques during this period. Though adsorption column chromatography has remained the mainstay for the separation and purification of the constituents in plant extracts, a broad range of chromatographic techniques such as HPLC and Liquid partition chromatography etc. make the isolation more rapid and efficient at present\textsuperscript{18}. Though natural products isolation still remains largely empirical and it requires experience as well as patience, with the availability of modern spectroscopic techniques, characterization of the isolates from plant extracts has become relatively simple and easy.

Bio-assay guided separation techniques have been proved to be beneficial and are relatively simple, rapid, reproducible and inexpensive. The techniques are not only sensitive enough to detect the active principles present in low concentration in the extracts but also selective to
avoid false positive and negative tests. Tannins, generally give such false positive tests and they have to be suitably removed before bio-assay is done. Once the active extracts are obtained, further fractionation is carried out to confirm the activity of pure active constituents. Though certain groups of compounds like flavonoids, triterpenoids etc. are considered to be ubiquitous in nature and hence pharmacologically unimportant, in recent years flavonoids have been found to be major constituents of many drugs of plant origin, where they contribute substantially to their curative effects. Pentacyclic triterpenoids like α-amyrin and lupeol are shown to exhibit distinct antibacterial activity$^{19}$. Oleanolic acid glycoside has been shown to be a new hypoglycemic agent$^{20}$ and betulin and its derivatives as anti HIV agents$^{21}$. In the light of these findings, it becomes imperative that herbal plants used in the system of native medicines are to be examined thoroughly for their phytoconstituents of all types.

A correlation between biological activity of medicinal plants and their use in traditional system of medicine has been demonstrated by phytochemists in several cases and more recently in the field of anticancer agents. While it is not possible to elevate every traditional remedy to the status of an established medicine in terms of modern scientific concepts, attempts are identified to prove the beneficial effects in the treatment of diseases like cancer, fertility control, inflammation, allergy, hepato-toxicity and CNS activity etc. Although plants are widely used, only a small percentage of higher plants have been investigated phytochemically and still only a smaller percentage is subjected to biological or pharmacological screening$^{22}$. 
Pharmacological studies of phytoconstituents have assumed a lot of significance in drug research, as combined efforts of pharmacognosists, phytochemists and pharmacologists has resulted in the development of newer drugs of varying structural features with promising therapeutic utility. Gupta has reviewed in detail the various perspectives of a number of medicinal plants\textsuperscript{24}. Opportunities for multidisciplinary research that links natural products chemistry, molecular and cellular biology, synthetic and analytical chemistry, biochemistry, pharmacognosy and pharmacology help to exploit the vast diversity of chemical structures and biological activities of natural products\textsuperscript{25}.

1.3 Review of literature

1.3.1 Pharmacognostical investigations of *Dalbergia* species

A systematic account of the genus *Dalbergia* in the Eastern Ghats, in which the description and distribution of seven plant species including *D. rubiginosa* in Andhra Pradesh for the first time has been reported by Murthy *et al*\textsuperscript{26}. Patil and Mahamulkar\textsuperscript{27} have reported nine taxa of the powdery mild dew fungi belonging to five genera, including a species of *Dalbergia* viz. *D. rubiginosa*. 
D. benthamaii Prain which is often confused with D. rubiginosa Roxb has been reported in the Indian subcontinent by Nair K.K.N\textsuperscript{28,29}, throwing light on the identity and distribution of the taxa of both the species. Sheikh et al., in their study on rate of growth of various plant species, have reported that the growth for D. malabarica was considerably better over a period of six years.

A thorough survey of literature shows that no systematic pharmacognostical investigation of any Dalbergia species has been carried out so far except the taxanomical work mentioned above.

1.3.2 Phytochemical investigations of Dalbergia species

Among higher plants, the family Leguminosae is a large one having more than 600 genera and 12,000 species. Plants belonging to this family vary in size from small shrubs and creepers to large trees. Dalbergia, an important genus of trees, shrubs and climbers, belonging to the family of Leguminosae and sub-family Papilionaceae, with about 120 species is scattered in the tropics and sub-tropics and also in the temperate parts of South East Asia and North Australia. Out of all the Dalbergia species available in the world, only 35 of them are reportedly present in India’. Dalbergia species have already been reported to possess a wide range of medicinal properties\textsuperscript{34}.

Thorough phytochemical examination of various species of Dalbergia has resulted in the isolation, characterization of a large number of compounds like flavonoids, isoflavonoids, neoflavonoids, steroids, terpenoids, etc and a number of reviews have been published on the phytochemical investigations of Dalbergia species\textsuperscript{36,39}. 
Flavonoids, which are generally phenolic in nature, are one of the most diverse and widespread groups of natural products. Flavonoids are a large group of over 4000 secondary plant metabolites\textsuperscript{40}. The relative stability, the wide distribution of flavonoids in green plants and their early identification have made flavonoids particularly useful as taxonomic markers in plant classification. In addition to this, flavonoids have been reported to be potent bioactive constituents showing a broad spectrum of biological activities\textsuperscript{41}. Flavonoids are also very useful in a number of ways such as in tanning of leather, as flavouring agents and also in the nutritional quality of food stuffs.

Flavonoids are generally present in plants in the free form (as aglycones) or bound to sugar(s) as glycosides. A flavonoid aglycone may occur in a single plant in several glycosidic combinations\textsuperscript{42}. Flavonoids occur in a variety of structural forms, which contain 15 carbon atoms in their nucleus and share the common structural feature of two phenyl rings linked by a three carbon chain (C\textsubscript{6}-C\textsubscript{3}-C\textsubscript{6}) as diphenyl propane derivatives.

Compounds like flavonoids, flavanoids, chalconoids and auroids possess a 1,3-diphenyl propane skeleton, compounds like isoflavonoids, 3-phenyl coumarins and pterocarpanoids possess a 1,2-diphenyl propane skeleton while compounds like neoflavonoids possess a 1,1-diphenyl propane skeleton.
The various flavonoid types present in *Dalbergia* species are given below:
The phytochemical investigations of *Dalbergia* species have been a subject of number of earlier reviews\(^{36,39}\) and the present review is a brief survey of the recent work done on the chemical components of *Dalbergia* in the last two decades. Herein various isoflavones, neoflavones, pterocarpans and steroids isolated from *Dalbergia* species since 1981 with respect to the source, isolates, structures and references are listed below.

1.3.2.1 Isoflavones and their glycosides isolated from *Dalbergia* species

The details isoflavones and their glycosides isolated from *Dalbergia* species are listed below:

| 1  | Formononetin (1) | D. candenatensis  
D. frutescens\(^{44}\)  
D. odorifera\(^{45,45}\)  
D. olivari\(^{47}\) |
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>2</td>
<td>Daidzein (2)</td>
<td>D. frutescens(^{44})</td>
</tr>
<tr>
<td>3</td>
<td>Castanin (3)</td>
<td>D. frutescens(^{44})</td>
</tr>
<tr>
<td>4</td>
<td>Odoratin (4)</td>
<td>D. frutescens(^{44})</td>
</tr>
<tr>
<td>5</td>
<td>Glycitein(5)</td>
<td>D. frutescens(^{44})</td>
</tr>
<tr>
<td>6</td>
<td>Pseudo baptagenin(6)</td>
<td>D. frutescens(^{44})</td>
</tr>
<tr>
<td>7</td>
<td>Fugikinetin(7)</td>
<td>D. frutescens(^{44})</td>
</tr>
<tr>
<td>8</td>
<td>Cuneatin (8)</td>
<td>D. frutescens(^{44})</td>
</tr>
<tr>
<td></td>
<td>Compound Description</td>
<td>Species</td>
</tr>
<tr>
<td>---</td>
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<td>------------------------</td>
</tr>
</tbody>
</table>
| 9 | Biochanin-A (9)                      | *D. frutescens*<sup>44</sup>  
|   |                                      | *D. olivari*<sup>47</sup>  
|   |                                      | *D. sissoides*<sup>48</sup>  
|   |                                      | *D. volubilis*<sup>49</sup>  |
| 10 | Biochanin-A-7-O-apisyl (1→6) glucoside (10) | *D. lanceolata*<sup>50</sup>  |
| 11 | Sissotrin (11)                        | *D. sissoides*<sup>51</sup>  |
| 12 | Tectorigenin (12)                     | *D. riparia*<sup>52</sup>  
|   |                                      | *D. sissoides*<sup>48</sup>  
|   |                                      | *D. sissoo*<sup>53</sup>  
|   |                                      | *D. volubilis*<sup>54</sup>  |
| 13 | Tectorigenin-7-O-gentiobioside (13)   | *D. sissoides*<sup>48</sup>  |
| 14 | 7-Methyl tectorigenin (14)            | *D. spinosa*<sup>55</sup>  |
| 15 | 7-Methyl tectorigenin-4'-O-β-galactoside (15) | *D. spinosa*<sup>55</sup>  |
| 16 | Dalspinosin (16)                      | *D. coromandeliana*<sup>56</sup>  
|   |                                      | *D. spinosa*<sup>57</sup>  |
| 17 | Junepeginin-B-7-O-glucoside (17)      | *D. spinosa*<sup>58</sup>  |
| 18 | Prunetin (18)                         | *D. spinosa*<sup>55</sup>  |
| 19 | Prunetin-4'-O-apisyl glucoside (19)   | *D. coromandeliana*<sup>59</sup>  |
| 20 | Prunetin-4'-O-β-D-galactoside (20)    | *D. spinosa*<sup>55</sup>  |
| 21 | Genistein (21)                        | *D. frutescens*<sup>11</sup>  
|   |                                      | *D. olivari*<sup>17</sup>  |
| 22 | 6,8-Bis-β-D-glucopyranosyl genistein (22) | *D. monetaria*<sup>60</sup>  |
| 23 | 3'-O-Methyl orobol (23)               | *D. paniculata*<sup>61</sup>  |
| 24 | 6-β-D-Glucopyranosyl orobol (24)      | *D. monetaria*<sup>60</sup>  |
| 25 | 8-(6"-O-Acetyl-β-D-glucopyranosyl) orobol (25) | *D. monetaria*<sup>60</sup>  |
| 26 | 6-(O-Acetyl-β-D-glucopyranosyl) orobol (26) | *D. monetaria*<sup>60</sup>  |
| 27 | 8-β-D-Glucopyranosyl orobol (27)      | *D. monetaria*<sup>60</sup>  |
| 28 | 6,8-Bis-C-glucopyranosyl orobol (28)  | *D. monetaria*<sup>60</sup>  |
| 29 | Caviunin (29)                         | *D. coromandeliana*<sup>77</sup>  
|   |                                      | *D. paniculata*<sup>61</sup>  
|   |                                      | *D. spinosa*<sup>55</sup>  |
| 30 | Dalpaniculin (30)                     | *D. paniculata*<sup>62</sup>  |
| 31 | Caviunin-7-O-rhamnoglucoside (31)     | *D. paniculata*<sup>62</sup>  |
| 32 | Caviunin-7-O-glucoside (32)           | *D. paniculata*<sup>62</sup>  |
| 33 | Isocaviunin (33)                      | *D. paniculata*<sup>62</sup>  |
| 34 | Isocaviunin-7-O-β-D-glucoside (34)    | *D. paniculata*<sup>62</sup>  |
| 35 | 3'-O-Methyl daidzein (35)             | *D. odorifera*<sup>64</sup>  |
| 36 | 3'-Hydroxy daidzein (36)              | *D. odorifera*<sup>55</sup>  |
### 1.3.2.2 Neoflavones Isolated from *Dalbergia* Species

The details of the neoflavones isolated from *Dalbergia* species are listed below:

<table>
<thead>
<tr>
<th></th>
<th>Neoflavone</th>
<th>Species</th>
</tr>
</thead>
<tbody>
<tr>
<td>37</td>
<td>Calycosin (37)</td>
<td><em>D. cochinchinesis</em></td>
</tr>
<tr>
<td>38</td>
<td>Bowdichione (38)</td>
<td><em>D. odorifera</em></td>
</tr>
<tr>
<td>39</td>
<td>5-Hydroxy bowdichione (39)</td>
<td><em>D. cadenatensis</em></td>
</tr>
<tr>
<td>40</td>
<td>Dalspinin (40)</td>
<td><em>D. coromandeliana</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>D. horrida</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>D. spinosa</em></td>
</tr>
<tr>
<td>41</td>
<td>Dalspinin-7-O-β-D-galactopyranoside (41)</td>
<td><em>D. spinosa</em></td>
</tr>
<tr>
<td>42</td>
<td>Dalpalatin (42)</td>
<td><em>D. paniculata</em></td>
</tr>
<tr>
<td>43</td>
<td>7-Hydroxy-2',4',5'-trimethoxy isoflavone (43)</td>
<td><em>D. monetaria</em></td>
</tr>
<tr>
<td>44</td>
<td>7-O-β-D-Glucopyranosyl-2',4',5'-trimethoxyisoflavone (44)</td>
<td><em>D. monetaria</em></td>
</tr>
<tr>
<td>45</td>
<td>Xenognosin B (45)</td>
<td><em>D. odorifera</em></td>
</tr>
<tr>
<td>46</td>
<td>2',7-Dihydroxy-4',5'-dimethoxy isoflavone (46)</td>
<td><em>D. odorifera</em></td>
</tr>
<tr>
<td>47</td>
<td>Sativanone (47)</td>
<td><em>D. odorifera</em></td>
</tr>
<tr>
<td>48</td>
<td>Koparin (48)</td>
<td><em>D. odorifera</em></td>
</tr>
<tr>
<td>49</td>
<td>5-Hydroxy-6,7-dimethoxy-4'-O-(6-O-apio-β-D-furanosyl-β-D-glucopyranosyl) isoflavone (49)</td>
<td><em>D. nigra</em></td>
</tr>
<tr>
<td>50</td>
<td>Biochanin-A-7-O-[-β-D-apio furanosyl-(1→6)-β-D-glucopyranosyl] (50)</td>
<td><em>D. sissoo</em></td>
</tr>
<tr>
<td>51</td>
<td>Tectorigenin-7-O-[-β-D-apio furanosyl-(1→6)-β-D-gluco pyranoside] (51)</td>
<td><em>D. sissoo</em></td>
</tr>
<tr>
<td>52</td>
<td>Olibergin A (52)</td>
<td><em>D. olivari</em></td>
</tr>
<tr>
<td>53</td>
<td>Olibergin B (53)</td>
<td><em>D. olivari</em></td>
</tr>
<tr>
<td>54</td>
<td>4',5',7-Triacetoxy-2'-methoxy isoflavone (54)</td>
<td><em>D. nitidula</em></td>
</tr>
</tbody>
</table>

1.3.2.2 Neoflavones Isolated from *Dalbergia* species
<table>
<thead>
<tr>
<th></th>
<th>Compound</th>
<th>Species</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>Isodalbergin (58)</td>
<td><em>D. sissoo</em></td>
</tr>
<tr>
<td>5</td>
<td>Melannein (59)</td>
<td><em>D. melanoxylon</em></td>
</tr>
<tr>
<td>6</td>
<td>Melannin (60)</td>
<td><em>D. melanoxylon</em></td>
</tr>
<tr>
<td>7</td>
<td>Stevenin (61)</td>
<td><em>D. odorifera</em></td>
</tr>
<tr>
<td>8</td>
<td>Sisafolin (62)</td>
<td><em>D. latifolia</em></td>
</tr>
<tr>
<td>9</td>
<td>Melanettin (63)</td>
<td><em>D. odorifera</em></td>
</tr>
<tr>
<td>10</td>
<td>3'-Hydroxy melanettin (64)</td>
<td><em>D. odorifera</em></td>
</tr>
<tr>
<td>11</td>
<td>Volubilin (65)</td>
<td><em>D. volubilis</em></td>
</tr>
<tr>
<td>12</td>
<td>Voludal (66)</td>
<td><em>D. volubilis</em></td>
</tr>
<tr>
<td>13</td>
<td>Seshadrin (67)</td>
<td><em>D. volubilis</em></td>
</tr>
</tbody>
</table>

### 1.3.2.3 Pterocarpan isolated from *Dalbergia* species

The details of pterocarpan isolated from *Dalbergia* species are listed below:

<table>
<thead>
<tr>
<th></th>
<th>Compound</th>
<th>Species</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Medicarpin (68)</td>
<td><em>D. odorifera</em></td>
</tr>
<tr>
<td>2</td>
<td>Methyl nissolin (69)</td>
<td><em>D. odorifera</em></td>
</tr>
<tr>
<td>3</td>
<td>Melitocarpan C (70)</td>
<td><em>D. odorifera</em></td>
</tr>
<tr>
<td>4</td>
<td>Melitocarpan D (71)</td>
<td><em>D. odorifera</em></td>
</tr>
<tr>
<td>5</td>
<td>Niliudecarpin (72)</td>
<td><em>D. malabarica</em></td>
</tr>
<tr>
<td>6</td>
<td>Odoricarpin (73)</td>
<td><em>D. odorifera</em></td>
</tr>
<tr>
<td>7</td>
<td>Melitocarpan A (74)</td>
<td><em>D. odorifera</em></td>
</tr>
<tr>
<td>8</td>
<td>3-Hydroxy-9-methoxy coumestan (75)</td>
<td><em>D. odorifera</em></td>
</tr>
</tbody>
</table>

### 1.3.2.4 Steroids isolated from *Dalbergia* species

The details of the steroids isolated from *Dalbergia* species are listed below:

<table>
<thead>
<tr>
<th></th>
<th>Compound</th>
<th>Species</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Campesterol (76)</td>
<td><em>D. monetaria</em></td>
</tr>
<tr>
<td>2</td>
<td>β-Sitosterol (77)</td>
<td><em>D. monetaria</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>D. paniculata</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>D. sissoides</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>D. volubilis</em></td>
</tr>
<tr>
<td>3</td>
<td>Stigmasterol (78)</td>
<td><em>D. monetaria</em></td>
</tr>
</tbody>
</table>

14
(1) \( R_1 = R_2 = R_3 = H, R_4 = CH_3 \)
(2) \( R_1 = R_2 = R_3 = R_4 = H \)
(3) \( R_1 = OCH_3, R_2 = R_3 = H, R_4 = CH_3 \)
(4) \( R_1 = OCH_3, R_2 = H, R_3 = OH, R_4 = CH_3 \)
(5) \( R_1 = OCH_3, R_2 = R_3 = R_4 = H \)
(6) \( R_1 = R_2 = H \)
(7) \( R_1 = OCH_3, R_2 = H \)
(8) \( R_1 = H, R_2 = OCH_3 \)
(9) \( R_1 = H, R_2 = OH \)
(10) \( R_1 = Apiosyl(1\rightarrow6) \text{ glucose}, R_2 = OH \)
(11) \( R_1 = Glucose, R_2 = OH \)
(12) \( R_1 = R_2 = H \)
(13) \( R_1 = Gentiobiose, R_2 = H \)
(14) \( R_1 = CH_3, R_2 = H \)
(15) \( R_1 = CH_3, R_2 = Galactose \)
(16) \( R_1 = H \)
(17) \( R_1 = Glucose \)
(18) $R_1 = H$
(19) $R_1 = \text{Apiosyl (1→6) glucose}$
(20) $R_1 = \text{Galactose}$

(21) $R_1 = R_2 = H$
(22) $R_1 = R_2 = \text{Glucose}$

(23) $R_1 = R_2 = H, R_3 = \text{CH}_3$
(24) $R_1 = R_3 = H, R_2 = \text{Glucose}$
(25) $R_1 = 6\''-\text{O-Acetylglucose}$
$R_2 = R_3 = H$

(26) $R_1 = H$
$R_2 = 6''\text{-O-Acetylglucose}$
(27) $R_1 = \text{Glucose}, R_2 = H$
(28) $R_1 = R_2 = \text{Glucose}$

(29) $R_1 = R_2 = H$
(30) $R_1 = \text{Glucose}, R_2 = H$
(31) $R_1 = H$
$R_2 = \text{Rhamnoglucose}$

(32) $R = \text{Glucose}$
(33) $R = H$
(34) $R = \text{glucose}$

(35) $R_1 = \text{CH}_3, R_2 = H$
(36) $R_1 = R_2 = H$
(37) $R_1 = H, R_2 = \text{CH}_3$

(38) $R_1 = H$
(39) $R_1 = \text{OH}$

(40) $R_1 = R_2 = H$
(41) $R_1 = \text{Galactose}, R_2 = H$
(42) $R_1 = H, R_2 = \text{OCH}_3$

(43) $R = H$
(44) $R = \text{Glucose}$

(45) $R_1 = R_2 = H$
(46) $R_1 = H, R_2 = \text{OCH}_3$
(47) $R_1 = \text{CH}_3, R_2 = H$
\[ (48) \]

\[ R_1 = H, R_2 = \text{OCH}_3, \quad R_3 = \text{Apioglucose} \]

\[ (49) \]

\[ R_1 = H, R_2 = \text{Apioglucose}, \quad R_3 = \text{CH}_3 \]

\[ (50) \]

\[ R = \text{O-APIoglucose} \]

\[ (51) \]

\[ (52) \]

\[ (53) \]

\[ (54) \]
(55) $R = CH_3, R_1 = H$
(56) $R = R_1 = CH_3$
(57) $R = R_1 = H$
(58) $R = H, R_1 = CH_3$

(59) $R = H, R_1 = OH$
(60) $R = OH, R_1 = OCH_3$
(61) $R = OH, R_1 = H$

(62) $H$

(63) $R_1 = R_2 = H$
(64) $R_1 = H, R_2 = OH$

(65) $R_1 = R_2 = H$
(66) $R_1 = CHO, R_2 = OCH_3$
(67) $R_1 = H, R_2 = OCH_3$
(68) \( R_1 = R_2 = H \)
(69) \( R_1 = H, R_2 = \text{OCH}_3 \)

(70) \( R = \text{OCH}_3 \)
(71) \( R = \text{OH} \)

(72)

(73) \( R_1 = \text{OCH}_3, R_2 = \text{OH} \)
(74) \( R_1 = \text{OH}, R_2 = H \)

(75)

(76)

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1.3.3 Pharmacological investigations of *Dalbergia* species

It is estimated that at least 25% of the population of the United States will face a cancer problem during their lifetime, with one million new cancer patients diagnosed every year. Less than a quarter of these patients will be cured solely by surgery and/or local radiation. Most of the remaining patients may receive systemic chemotherapy at sometime or the other during their illness. *Dalbergia* species with cancer chemopreventive activity have been studied in detail and five such cinnamyl phenols (1,3-diphenyl propenes) are reported to be isolated from *Dalbergia* species\(^8\).\(^6\)

Cheng *et al*\(^1\) reported the antioxidant property of butein, isolated from *D. odorifera* and butein serves as a powerful antioxidant against lipid as well as LDL peroxidation by its versatile free radical scavenging actions and metal ion chelation. Three flavonoids isolated from the heartwood of *D. odorifera* were reported to possess anti-allergic and anti-inflammatory activities\(^8\)\(^8\). Prostaglandins and leucotrienes are released by a host of mechanical, thermal, chemical, bacterial and other insults and they contribute mainly to the genesis of the signs and symptoms of
inflammation\textsuperscript{80,91}. The methylene chloride extract of \textit{D. odorifera} is reported to be a potent inhibitor of LTC\textsubscript{4}, formation in mastocytoma cells\textsuperscript{92}.

Antiandrogens like finasteride inhibit 5-\textit{oc} reductase that converts testosterone into its metabolite 5-\textit{oc} dihydrotestosterone (5-\textit{oc} DHT)\textsuperscript{93}. Four new compounds, in addition to the eight known phenolic compounds, isolated from the stem of \textit{D. cochinchinensis}, showed potent inhibitory effects towards 5-\textit{oc} DHT\textsuperscript{66}. Peters \textit{et al}\textsuperscript{9A} carried out embryo fetotoxicity studies of stem bark decoction of \textit{D. subcymosa} using Wistar rats and Dalsaxini, a glycoside isolated from the root of \textit{D. saxatilis} has been reported to cause rat uterine muscle contraction by mobilizing Ca\textsuperscript{2+} through predominantly a voltage-dependent Ca\textsuperscript{2+} channel\textsuperscript{95}.

Yu \textit{et al} reported that butein, isolated from \textit{D. odorifera} caused endothelium-dependent relaxation of rat aorta that was precontracted with phenylephrine. Isoliquiritigenin, isolated from \textit{D. odorifera} is a novel soluble guanylate-cyclase activator and is reported to induce vasorelaxant effect on rat aorta that was precontracted with phenylephrine\textsuperscript{97}. Colony stimulating factor (CSF) is a hematopoietic growth factor in human body. It stimulates monocyte/macrophage colony formation, enhances production of interferon and tumour necrosis factor and enhances functions of monocyte and macrophages\textsuperscript{98}. Hot aqueous extract of \textit{D. monetaria} reportedly exhibits very high CSF-inducing activity

The results of antimicrobial activity of \textit{D. melanoxyylon} extract reported by Gundidza \textit{et al}\textsuperscript{100} have shown that the ethanolic extract of leaves of \textit{D. melanoxyylon} showed significant antibacterial effect. Four
flavonoids isolated from the heartwood of *D. louvelii* showed significant antiplasmodial activity against *Plasmodium falciparum*101.

The use of extracts of *Dalbergia* species is reported for the treatment of arthritis, gonorrhoea and rheumatism102. *D. sissoo*, *D. lanceolaria*, *D. nigra*, *D. parviflora* and *D. volubilis* are reported, in general to possess a number of medicinal properties including antimicrobial activity104. The leaves of *D. lanceolaria* are used in the treatment of arthritic disabilities105 and that of *D. nigra* are claimed to possess antibiotic potency106. The aqueous extract of *D. parviflora* is reported to be a blood tonic and secretolyte, whereas the oil obtained from *D. parviflora* is found to be curative in ulcerated wound107. The extracts of leaves of *D. volubilis* showed significant anti-inflammatory and antiarthritic activity in rats108.

The isolates from the heartwood of *D. odorifera*, inhibited the prostaglandin biosynthesis as well the platelet aggregation induced by arachidonic acid109110. Medicarpin, an isolate from the wood of *D. monetaria* was shown to possess high antifungal, antibacterial activities and also high anti-feedon activity against cotton-ball weevil111. The binary flavonoids isolated from the roots of *D. odorifera* exhibited antilipidemic properties and reduced cholesterol level in serum117.

The heartwood of *D. odorifera* has been used in traditional Chinese medicine to treat blood disorders, ischemia and inflammation113. The methanol extract of *D. odorifera* heartwood has been shown to be effective against hypercholesterolemia114,115. A patented pharmaceutical formulation of *D. hencei* with other plant drugs is available for transdermal application in the treatment of coronary heart disease116.

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The toxicity of ethanol:water (1:1) extract of *D. rubiginosa* was studied by Bhakuni *et al* who carried out only the assessment of toxicity quantitatively and the LD$_{50}$ was reported as 750 mg/kg. Ethanolic extract of dried aerial parts of *D. rubiginosa* was screened for insecticidal activity and it was found inactive. Biochanin-A, an isoflavone isolated from the flowers of *D. sissoides* has been reported to possess significant antitumour activity against Dalton’s ascitic lymphoma and larvicidal activity.

Petroleum ether extract of stem bark of *D. malabarica* showed significant CNS depressant activity. Two isoflavonoids, namely Olibergin A and B isolated from the stem bark of *D. olivari* by Chihiro Ito *et al* have been reported to possess antitumour activity. The ethanolic extract of *D. sissoides* pods revealed significant antiulcer activity by reducing the ulcer index and preventing the gastric mucous erosion against pylorus ligated model.

1=4 Aim and scope of the present study

Flavonoids, synthesized in plants nearly to an extent of 0.5 to 1.5%, are reported for diversified biological effects like anti-inflammatory, antioxidant, antimicrobial, antineoplastic etc. *Dalbergia* is an important source of flavonoids, isoflavonoids, neoflavonoids, steroids, terpenoids etc.

Detailed survey of literature shows that though some phytochemical work has been carried out on *D. malabarica*, no such work is reported with *D. rubiginosa*. No pharmacognostical and pharmacological work have been reported so far on both the *Dalbergia* species selected for our study. The quantitative toxicity assessment for
D. rubiginosa has been carried out by Bhakuni et al.\textsuperscript{17} only to complete the study of insecticidal activity.

On the basis of the above considerations, the current focusing of world’s attention towards sphere of alternative system of medicine and the importance of flavonoids as curative measures in diverse ailments, we have taken up two species of Dalbergia namely, Dalbergia malabarica Prain and Dalbergia rubiginosa Roxb to have a holistic approach with a idea of carrying out detailed pharmacognostical, phytochemical and pharmacological studies. As a part of this approach, we have carried out a systematic pharmacognostical study to standardize the plant species and to localize the types of phytoconstituents present, to isolate and characterize them and also to identify the pharmacological activities of the plant extracts as well as the isolates.
References


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