CHAPTER - I

Introduction

Phytochemical consideration of the constituents of the order Rutales

The present thesis relates to chemical investigation of Indian medicinal plants of the order Rutales. A short review on the botanical and chemical aspect of this order is presented in this chapter. The review of the chemistry of the order will be presented from comparative phytochemical stand point.

According to Engler and Diels\(^1\) the large order Geraniales consisted of twenty one families. Rendle\(^2\), from morphological and anatomical consideration considered the families Rutaceae, Simaroubaceae, Burseraceae and Meliaceae distinctly different from other families and segregated into a smaller order, Rutales. This narrower circumspection in principle has also been advocated by Hutchinson\(^3\). But Hutchinson excludes Meliaceae and includes Averrhoaceae in his Rutales. Engler and Melchior\(^4\) have recognised the order Rutales as a separate one.
In Table 1 the members of the constituent families of the order Rutales as advocated by different authors have been detailed together with members of the larger order Geraniales as advocated by Engler and Prantl.

Table 1: Segregated order Rutales

<table>
<thead>
<tr>
<th>Order</th>
<th>Families</th>
<th>Related to</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rutales</td>
<td>Rutaceae</td>
<td>Geraniales</td>
<td>Rendle(^2)</td>
</tr>
<tr>
<td></td>
<td>Simaroubaceae</td>
<td>(in Hutchinson's</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Herbaceae)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Burseraceae</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Meliaceae</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rutales</td>
<td>Rutaceae</td>
<td></td>
<td>Engler and</td>
</tr>
<tr>
<td></td>
<td>Cenoraceae</td>
<td></td>
<td>Diels(^1)</td>
</tr>
<tr>
<td></td>
<td>Burseraceae</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Simaroubaceae</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Picrodendraceae</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Meliaceae</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Akaniaeae</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Malpighiaceae</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Trigonieae</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vochysiaceae</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tremandraceae</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Polygalaceae</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rutales</td>
<td>Rutaceae</td>
<td>Far away from</td>
<td>Hutchinson(^3)</td>
</tr>
<tr>
<td></td>
<td>Simaroubaceae</td>
<td>Geraniales in his</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Averrhoaceae</td>
<td>lignosae</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Burseraceae</td>
<td>closer to Celastrales</td>
<td></td>
</tr>
</tbody>
</table>
The phyletic status of the order as proposed by Rendle, Engler and Diels places the order near Geraniales while Hutchinson places it in his lignosae far away from Herbaceous Geraniales. The phyletic status of the order as proposed by Hutchinson\(^3\) is shown in Fig. 1 below.

![Fig. 1. Phylogeny of the order Rutales.](image)

This disputed taxonomically status of the order Rutales cannot so easily be resolved by morphologically based evolutionary concepts. Further, it has always been a disputed observation whether these morphological homologies reflect the phylogenetic relationship in convergent or parallel evolution. In such controversial situations some other parameters have been sought to test the validity of the phylogenetic scheme based on morphology. The
anatomical, cytological, embryological biochemical and other parameters have aided to the understanding of the evolutionary status of plants.

It follows from the recent understanding of the comparative phytochemistry that the plants at a similar phyletic level should elaborate secondary constituents of similar biogenetic origin. The developments in the area of biogenesis of natural products have aided this concept of comparative phytochemistry. The occurrence of a particular type of secondary constituents in a closely related groups speaks of similar enzymatic make up of the plants. This presupposes that the production of the secondary constituents is gene controlled. These constituents, may, therefore, be taken at a particular level of comparison of the genetic make up or phyletic status of plants. In short the secondary constituents is an expression of the biochemical profile of the plant.

It is evident that there is some difference of opinion as to the taxonomic status of the order Rutales, the analysis of the chemical constituents in consideration of the biogenetic relationship may be helpful in solving the problem.

In consideration of the biogenesis of the aromatic and terpenic constituents of the family the compounds may be classified as follows:
(a) Aromatics including those with a fragment derived from a MU unit.
(b) Terpenoids

The aromatics consist of alkaloids, amides, coumarins, flavonoids while the terpenoids belong to the limonoids, meliacins and quassinoid groups.

The aromatics of the family could be divided into two categories.
(a) Those originating via Shikimateanthranilate pathway mainly alkaloids.
(b) Those originate from Shikimateprephenate pathway. They include alkaloids or oxygen heterocyclics or lignans originating via prephenic acid.

The biosynthesis of all the aromatic constituents of the order could be shown to arise schematically as follows.
Fig. 2. Probable biogenetic pathways of some alkaloids and Coumarins of the family Rutaceae.
The alkaloids of anthranilic acid origin was considered very characteristic for the family Rutaceae by Price. The following types of alkaloids are considered derived from anthranilic acid.

(a) Simple anthranilic acid and its derivatives (I).
(b) Quinoline alkaloids (II).
(c) Quinoline alkaloids with furan and pyran rings (III & IV).
(d) Quinazoline alkaloids (V).
(e) Indoloquinoline alkaloids (VI).
(f) Acridine alkaloids (VII).
(g) Simple and pyranocarbazole derivatives (VIII & IX).

\[
\begin{align*}
(I) & \quad \text{Simple anthranilic acid and its derivatives} \\
(II) & \quad \text{Quinoline alkaloids} \\
(III) & \quad \text{Quinoline alkaloids with furan and pyran rings} \\
(IV) & \quad \text{Indoloquinoline alkaloids}
\end{align*}
\]
The alkaloids with a pyran or furan ring fused to it (e.g. furoquinoline, pyranoquinoline and pyranoacridones) have been reported. They are very characteristic for the family. The pyran or furan fragment are contributions of the mevalonate pathway. From biogenetic considerations they may be considered as aromatics with modified mevalonate unit. This group also includes compounds with C_{5}, C_{10} or C_{15} unit incorporated into an alkaloidal or coumarinic fragment.
The following table shows an illustration of typical members of compounds which could arise from anthranilic acid.

Table 2: Some typical structural representative of alkaloids present in Rutaceae

<table>
<thead>
<tr>
<th>Name &amp; molecular formula</th>
<th>Structure</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple anthranilic acid derivative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Methyl anthranilate$^9$</td>
<td><img src="image" alt="Structure of Methyl Anthranilate" /></td>
<td>Citrus sp.</td>
</tr>
<tr>
<td>$C_8H_9NO_2$</td>
<td></td>
<td>Eriosteman sp.</td>
</tr>
<tr>
<td>Simple quinoline derivative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Flindersine$^{10}$</td>
<td><img src="image" alt="Structure of Flindersine" /></td>
<td>Flindersia australis</td>
</tr>
<tr>
<td>(1)</td>
<td>(2)</td>
<td>(3)</td>
</tr>
<tr>
<td>-----</td>
<td>-----</td>
<td>-----</td>
</tr>
<tr>
<td>1. Melicopicine&lt;sup&gt;12&lt;/sup&gt;</td>
<td><a href="#">Structure</a></td>
<td>Melicope fareana</td>
</tr>
<tr>
<td>C&lt;sub&gt;18&lt;/sub&gt;H&lt;sub&gt;19&lt;/sub&gt;N&lt;sub&gt;5&lt;/sub&gt;O&lt;sub&gt;5&lt;/sub&gt; (XIII)</td>
<td><a href="#">Structure</a></td>
<td></td>
</tr>
</tbody>
</table>

Acridone alkaloids

2. Oricine<sup>11</sup> | [Structure](#) | Oricia sauveolens |
| C<sub>18</sub>H<sub>22</sub>N<sub>4</sub>O<sub>4</sub> (XII) | [Structure](#) |  |

2. Atalaphylline<sup>13</sup> | [Structure](#) | Atalantia monophylla |
| C<sub>23</sub>H<sub>25</sub>N<sub>4</sub>O<sub>4</sub> (XIV) | [Structure](#) |  |
### Table 2 (contd.)

<table>
<thead>
<tr>
<th></th>
<th>(1)</th>
<th>(2)</th>
<th>(3)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Furoquinoline alkaloids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td>Medicosmine$^{14}$</td>
<td>Medicosma</td>
<td>Cunninghamii</td>
</tr>
<tr>
<td></td>
<td>$C_{17}H_{15}NO_3$</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(XV)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Maculine$^{15}$</td>
<td>Flindersia</td>
<td>dissosperma</td>
</tr>
<tr>
<td></td>
<td>$C_{13}H_{9}NO_4$</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(XVI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Kokusagine$^{16}$</td>
<td>Lunasia</td>
<td>amara</td>
</tr>
<tr>
<td></td>
<td>$C_{13}H_{9}NO_4$</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(XVII)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 2 (contd.)

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)</td>
<td>(2)</td>
<td>(3)</td>
</tr>
<tr>
<td>4. Acronidine$^{17}$</td>
<td>Acronychia baucri</td>
<td></td>
</tr>
<tr>
<td>$C_{18}H_{17}NO_4$</td>
<td>Glycosmis arborea</td>
<td></td>
</tr>
<tr>
<td>(XVIII)</td>
<td>Skimmia repens</td>
<td></td>
</tr>
</tbody>
</table>

5. Skimmianine$^{18}$

$C_{14}H_{13}NO_4$

(XIX)
### Table 2 (contd.)

<table>
<thead>
<tr>
<th>(1)</th>
<th>(2)</th>
<th>(3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quinazoline alkaloids</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. Arborine\(^{19,20}\)  
C\(_{16}H_{14}N_{2}O\)  
(XX)  

![Arborine](image1.png)  
Glycosmis arborea

2. dl-vasicine\(^{21}\)  
C\(_{11}H_{12}N_{2}O\)  
(XXI)  

![dl-vasicine](image2.png)  
Adhatoda vasica  
Peganum harmala

3. Hortiamine\(^{22}\)  
C\(_{20}H_{17}N_{3}O_{2}\)  
(XXII)  

![Hortiamine](image3.png)  
Hortia arborea
A large number of alkaloids of the family Rutaceae which are derived from the shikimate pathway are of non-anthranilate origin. Members of the proto-berberine and benz-c-phenanthridine belong to this group.

The prephenate pathway gives rise to isoquinoline and some coumarins including terpenoid coumarins. The biosynthetic work of berberine and related alkaloids have been extensively studied and it has been proved that phenylalanine is the precursor of these alkaloids. Some of the aromatic amides owe their origin to the prephenate pathway. Typical examples of these members are shown below.

**Table 3: Typical members of alkaloids of non-anthranilate origin**

<table>
<thead>
<tr>
<th>Name and molecular formula</th>
<th>Structure</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) (2) (3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isoquinoline alkaloids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. N-methyl isocorydine</td>
<td><img src="image_url" alt="Structure" /></td>
<td>Fagara cocogill Eugl</td>
</tr>
<tr>
<td>chloride</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C_{21}H_{26}ClO_{4}N</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(XXIII)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 3 (contd.)

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Palmatine $^{28}$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$C_{21}H_{23}O_5N$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(XXIV)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Phellodendron amurense Rupf.

Table 4: Amides of Rutaceae

<table>
<thead>
<tr>
<th>Name and molecular formula</th>
<th>Structure</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Casimiroin $C_{12}H_{11}NO_4$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(XXV)</td>
<td></td>
<td>Casimoria Llave et Lex</td>
</tr>
<tr>
<td>(1)</td>
<td>(2)</td>
<td>(3)</td>
</tr>
<tr>
<td>-----</td>
<td>-----</td>
<td>-----</td>
</tr>
<tr>
<td>2. Aegeline</td>
<td><img src="image" alt="Aegeline molecule" /></td>
<td>Aegle marmelos Corr</td>
</tr>
<tr>
<td>C_{18}H_{19}N_{3}O_{3}</td>
<td>(XXVI)</td>
<td></td>
</tr>
<tr>
<td>3. Fagaramide</td>
<td><img src="image" alt="Fagaramide molecule" /></td>
<td>Fagara Zanthoxylum des Lam</td>
</tr>
<tr>
<td>C_{14}H_{17}N_{3}O_{3}</td>
<td>(XXVII)</td>
<td></td>
</tr>
<tr>
<td>4. Neoherculin</td>
<td><img src="image" alt="Neoherculin molecule" /></td>
<td>Zanthoxylum elavalherculis Piperatum</td>
</tr>
<tr>
<td>C_{16}H_{25}NO</td>
<td>(XXVIII)</td>
<td></td>
</tr>
</tbody>
</table>
Besides the alkaloids of shikimate pathway members of the imidazole group of alkaloids of the family Rutaceae have also been reported. Ornithine and histidine have been considered precursor of pyrrolidine and imidazole bases respectively while nicotinic acid could be considered as the precursor of pyridine bases. The combined shikimate and nicotinic acid pathway would be considered to operate in the iso-oxazoles.

Table 5: Pyrrolidine and imidazole alkaloids

<table>
<thead>
<tr>
<th>Name and molecular formula</th>
<th>Structure</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) (2) (3)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Pyrrolidine alkaloids

1. L-Stachydrine

\[ \text{C}_7\text{H}_{13}\text{N}_2 \text{O}_2 \]

(XXIX)
Table 5 (contd.)

<table>
<thead>
<tr>
<th>(1)</th>
<th>(2)</th>
<th>(3)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Imidazole alkaloids</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. Pilocarpine $^{31}$
   \[ C_{11}H_{16}N_2O_2 \]
   \[ (XXX) \]
   \[ \text{Pilocarpus jaborandi Holmes} \]

2. N-methyl halfordium chloride $^{33}$
   \[ C_{20}H_{24}N_2O_4Cl \]
   \[ (XXXII) \]
   \[ \text{Halfordia scleroxyla} \]

**Oxazole**

1. Aegelinine $^{32}$
   \[ C_{14}H_{10}N_2O_2 \]
   \[ (XXXI) \]
   \[ \text{Aegle marmelos Correa} \]
From Rutaceous plants simple coumarins, furocoumarins, chromeno-α-pyrone, coumarins with a side chain of C$_5$ and C$_{10}$ units have been reported. It has been reported that shikimic acid, phenylalanine and cinnamic acid are the precursor of Coumarin. Though the formation of C$_6$-C$_3$ unit is understood fairly well, yet the process of lactonisation of the cinnamic acid derivative to coumarin has been the subject of speculations and biosynthetic investigations. From the results of Brown on the biogenesis of umbelliferone the present day picture may schematically be shown as follows (XXXIII-XXXV).
Austin and Mayer put forward the views that O-glucosylation of the product of enzymic orthohydroxylation of trans-cinnamic acid system plays a key part in the ensuing stereomutation of the Cis-O-glycoside. The detection of an isomerase enzyme which converts trans-cinnamic acid to cis-cinnamic acid stands in favour of this concept that the plant contains an isomerase enzyme which converts the trans-cinnamic acid to coumarin in Melilotus alba. Furocoumarins and Chromeno-α-pyrones arise by further incorporation of a C₅-unit and subsequent cyclisation (XXXVI-XXXIX).
Typical structural representative of coumarins in Rutaceae are listed in Table 6.

Table 6: Typical structural representative of coumarins present in Rutaceae

<table>
<thead>
<tr>
<th>Name and molecular formula</th>
<th>Structure</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)</td>
<td>(2)</td>
<td>(3)</td>
</tr>
<tr>
<td>Citrus aurantifolium Linn.</td>
<td><img src="image" alt="Structure of Aurapteneol" /></td>
<td>Citrus aurantifolium Linn.</td>
</tr>
<tr>
<td>C_{15}H_{16}O_{4}</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(XL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toddalea aculeata Pers.</td>
<td><img src="image" alt="Structure of Toddaculine" /></td>
<td>Toddalea aculeata Pers.</td>
</tr>
<tr>
<td>C_{16}H_{16}O_{4}</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(XLI)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

7686
<table>
<thead>
<tr>
<th>(1)</th>
<th>(2)</th>
<th>(3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3. Coumurrayin&lt;sup&gt;39&lt;/sup&gt;</td>
<td><img src="image1" alt="Chemical Structure" /></td>
<td>Murraya exotica</td>
</tr>
<tr>
<td>C&lt;sub&gt;16&lt;/sub&gt;H&lt;sub&gt;18&lt;/sub&gt;O&lt;sub&gt;4&lt;/sub&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(XLII)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| 4. Phebalosin<sup>40</sup> | ![Chemical Structure](image2) | Phebalium tuberculofum Benth. |
| C<sub>15</sub>H<sub>14</sub>O<sub>4</sub> | | P. drummondii Benth. |
| (XLIII) | | |

| 5. 7-demethyl suberosin<sup>41</sup> | ![Chemical Structure](image3) | Koster Swietenia |
| C<sub>14</sub>H<sub>14</sub>O<sub>3</sub> | | |
| (XLIV) | | |
Table 6 (contd.)

<table>
<thead>
<tr>
<th>(1)</th>
<th>(2)</th>
<th>(3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6. Suberenol\textsuperscript{42}</td>
<td>(\text{Zanthoxylum suberosum})</td>
<td></td>
</tr>
<tr>
<td>(\text{C}<em>{15}\text{H}</em>{16}\text{O}_4)</td>
<td>(\text{C}<em>{14}\text{H}</em>{12}\text{O}_6)</td>
<td>(\text{Halfordia scaleroxyla F. Muell})</td>
</tr>
<tr>
<td>(XLV)</td>
<td>(XLVI)</td>
<td>(XLVII)</td>
</tr>
</tbody>
</table>

6. Suberenol\textsuperscript{42} \(\text{C}_{15}\text{H}_{16}\text{O}_4\) (XLV)

7. Halfordin\textsuperscript{43} \(\text{C}_{14}\text{H}_{12}\text{O}_6\) (XLVI)

8. Isohalfordin\textsuperscript{43} \(\text{C}_{14}\text{H}_{12}\text{O}_6\) (XLVII)
<table>
<thead>
<tr>
<th>(1)</th>
<th>(2)</th>
<th>(3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9. Dentatin$^{44,45}$</td>
<td>Clausena dentata</td>
<td>Clausena dentata C. heptaphylla</td>
</tr>
<tr>
<td>$C_{20}H_{22}O_4$</td>
<td>(XLVIII)</td>
<td></td>
</tr>
<tr>
<td>10. Murrayatin$^{46}$</td>
<td>Murraya exotica Linn.</td>
<td>Murraya exotica Linn.</td>
</tr>
<tr>
<td>$C_{20}H_{26}O_6$</td>
<td>(XLIX)</td>
<td></td>
</tr>
<tr>
<td>11. Xanthyletin$^{47}$</td>
<td>Clausena dentata</td>
<td>Clausena dentata</td>
</tr>
<tr>
<td>$C_{14}H_{12}O_3$</td>
<td>Wild</td>
<td>Wild</td>
</tr>
<tr>
<td>(L)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Flavonoids constitute another interesting group of plant heterocycles which has been extensively used in the chemotaxonomic analysis. The polymethoxy flavones are very common. The hydroxylation pattern of these flavonoids according to Geissman shows that similar plants perform the same kind of reaction producing flavonoids of similar hydroxylation pattern. Some typical representative flavonoids of the family Rutaceae are shown in Table 7.
Table 7: Some representative flavonoids of the family Rutaceae

<table>
<thead>
<tr>
<th>Name and molecular formula</th>
<th>Structure</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Zanthoxylum phosphodium</td>
<td>(3) Zanthoxylum thopodium</td>
<td>(LIII)</td>
</tr>
<tr>
<td>2,5:6-dimethoxy flavone</td>
<td>(2)</td>
<td>(LII)</td>
</tr>
<tr>
<td>C_{18}H_{16}O_{7}</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. Tambulin<sup>50</sup>

2. 5:6-dimethoxy<sup>51</sup> flavone

C_{17}H_{14}O_{4}

(LIII)
Table 7 (contd.)

<table>
<thead>
<tr>
<th>(1)</th>
<th>(2)</th>
<th>(3)</th>
</tr>
</thead>
</table>

3. Hibiscetin\(^{52}\)  
\[\text{C}_{15}\text{H}_{10}\text{O}_{9}\]  
(LIV)  

4. Hibiscetin heptamethyl ether\(^{53}\)  
\[\text{C}_{21}\text{H}_{24}\text{O}_{9}\]  
(LV)

5. Exoticin\(^{54}\)  
\[\text{C}_{23}\text{H}_{26}\text{O}_{10}\]  
(LVI)

\text{Murraya exotica Linn.}
<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)</td>
<td>(2)</td>
<td>(3)</td>
</tr>
<tr>
<td>6. Nobiletin&lt;sup&gt;55&lt;/sup&gt;</td>
<td><img src="image1" alt="Nobiletin Structure" /></td>
<td><em>Citrus nobilis</em></td>
</tr>
<tr>
<td>$C_{21}H_{22}O_8$</td>
<td>(LVII)</td>
<td></td>
</tr>
<tr>
<td>7. Auranetin&lt;sup&gt;56&lt;/sup&gt;</td>
<td><img src="image2" alt="Auranetin Structure" /></td>
<td><em>Citrus aurantium</em></td>
</tr>
<tr>
<td>$C_{20}H_{20}O_7$</td>
<td>(LVIII)</td>
<td></td>
</tr>
<tr>
<td>8. Ternatin&lt;sup&gt;57&lt;/sup&gt;</td>
<td><img src="image3" alt="Ternatin Structure" /></td>
<td><em>Melicope teruata</em></td>
</tr>
<tr>
<td>$C_{19}H_{16}O_8$</td>
<td>(LIX)</td>
<td></td>
</tr>
</tbody>
</table>
A new group of terpenoid heterocyclic compound has evoked widespread attention. Limonin (LX) is the first member of the series. This has initiated the investigations on a large number of this group of plant constituents.

The members of the group have been divided into limonoids and meliacins. Simaroubaceae bitter constituents may be added to this member. The precursor of limonin, according to Arigoni is conceived to be derived from tetracyclic triterpene euphol (LXI) or its congener. The furan ring originates from the side chain. The formation of the six membered lactone has been envisaged by Bayer-Villiger oxidation of ring D-ketone (LXII) to give the ring D-lactone (LXIII). Excellent precedent for C$_3$-C$_4$ biogenetic
cleavage of the triterpenoid skeleton has recently been revealed in the structure of nyctanthonic acid (LXIV) and damarenolic acid (LXV). Nortriterpenes with C_{26} are obtained from a tetracyclic triterpene by appropriate cleavage and migration. This may be schematically shown below.
In the Table 8 the limonin and some congeners of the family Rutaceae are listed:

<table>
<thead>
<tr>
<th>Name and molecular formula</th>
<th>Structure</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Limonin</strong>&lt;sup&gt;58&lt;/sup&gt;</td>
<td><a href="#">Structure image</a></td>
<td><em>Citrus species</em></td>
</tr>
<tr>
<td>( \text{C}<em>{26}\text{H}</em>{30}\text{O}_{8} )</td>
<td>( \text{LXVII} )</td>
<td></td>
</tr>
<tr>
<td><strong>2. Calodendrolide</strong>&lt;sup&gt;59&lt;/sup&gt;</td>
<td><a href="#">Structure image</a></td>
<td><em>Calodendrum</em></td>
</tr>
<tr>
<td>( \text{C}<em>{15}\text{H}</em>{16}\text{O}_{4} )</td>
<td>( \text{LXVII} )</td>
<td></td>
</tr>
</tbody>
</table>
Table 8 (contd.)

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>3. Citroline 60</td>
<td>C_{26}H_{28}O_{6}</td>
<td>Citrus species</td>
</tr>
<tr>
<td></td>
<td>(LXVIII)</td>
<td></td>
</tr>
<tr>
<td>4. Veprisone 61</td>
<td>C_{27}H_{34}O_{8}</td>
<td>Vepris bilocularis</td>
</tr>
<tr>
<td></td>
<td>(LXIX)</td>
<td></td>
</tr>
<tr>
<td>5. Fraxinellone 62</td>
<td>C_{14}H_{16}O_{3}</td>
<td>Dictamuns calodendrum</td>
</tr>
<tr>
<td></td>
<td>(LXX)</td>
<td></td>
</tr>
</tbody>
</table>
Recent addition to this nortriterpene is the penta nortriterpenoid, clausenolide\textsuperscript{64} (LXXII). The biogenesis of the hemiacetal, in the cleaved ring A, of (LXXII) has been conceived from oxidation product of deacetylnomilinic acid type compound (LXXIII) by decarboxylation and ring closure as envisaged below.
Deacetylnomilinic acid was isolated from citrus species by Raymond as early as 1971. The occurrence of Clausenolide shows that a key role is played by deacetylnomilin in the biogenesis of cleaved ring A of the limonoids.

The limonoïds of the family Rutaceae is characterised by the presence of a cleaved ring A, ring D and a furan ring. Meliacins on the other hand have $\beta$-substituted furan, ring A in
The cleavage of ring D, B and C are often met with. Some representative members of the degraded terpenoids of the family Meliaceae usually known as meliacins are tabulated in Table 9.

Table 9: Typical representative members of meliacins

<table>
<thead>
<tr>
<th>Name and molecular formula</th>
<th>Structure</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Khivorin</td>
<td><img src="image" alt="Khivorin Structure" /></td>
<td>Khaya ivoransis</td>
</tr>
<tr>
<td>C_{32}H_{42}O_{10} (LXXIV)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Methyl angolensate</td>
<td><img src="image" alt="Methyl angolensate Structure" /></td>
<td>Cedrela odorata</td>
</tr>
<tr>
<td>C_{27}H_{34}O_{7} (LXXV)</td>
<td></td>
<td>C. mexicana Entandrophragma angolense</td>
</tr>
</tbody>
</table>
Table 9 (contd.)

<table>
<thead>
<tr>
<th>(1)</th>
<th>(2)</th>
<th>(3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3. Gedunin$^{71,72}$</td>
<td><img src="" alt="Chemical Structure" /></td>
<td>Entandrophragma angolense</td>
</tr>
<tr>
<td>$C_{28}H_{34}O_7$</td>
<td><img src="" alt="Chemical Structure" /></td>
<td></td>
</tr>
<tr>
<td>(LXXVI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Nimbin$^{73}$</td>
<td><img src="" alt="Chemical Structure" /></td>
<td>Azadirachta indica</td>
</tr>
<tr>
<td>$C_{30}H_{36}O_9$</td>
<td><img src="" alt="Chemical Structure" /></td>
<td></td>
</tr>
<tr>
<td>(LXXVII)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Mahoganin$^{74}$</td>
<td><img src="" alt="Chemical Structure" /></td>
<td>Swietenia mahagoni Jacq.</td>
</tr>
<tr>
<td>$C_{27}H_{36}O_8$</td>
<td><img src="" alt="Chemical Structure" /></td>
<td></td>
</tr>
<tr>
<td>(LXXVIII)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Further degradation of the meliacin type of compound have been found in the members of the family Simaroubaceae. The formation of the Simaroubaceae bitter constituents has been conceived by Bredenberg, Dreyer and Halsall independently that limonoids or meliacins like Khivorin (LXXIV) on treatment with base undergoes hydrolysis and looses $\beta$-furfuraldehyde to give Khivol (LXXX) which apart from the extra carbon at $C_4$ has the same carbon skeleton and the same type of lactone ring and arrangements of atoms of ring as may be found in glaucarubol (LXXXI). It is interesting whether the stereochemistry at $C_7$ and $C_8$ in these diterpenes is the same as Khivol (LXXX) and whether $C_{11}$ and $C_{12}$ both arise from the carboxyl carbon of acetic acid.

### Table 9 (contd.)

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>6. Andirobin$^{75}$</td>
<td>Carana guayanesis</td>
<td></td>
</tr>
<tr>
<td>$C_{27}H_{32}O_7$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(LXXIX)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Some representative members of the terpenoids and nor-terpenoids of the family simaroubaceae are listed in Table 10.
Table 10: Typical representative members of nor-triterpenoids of Simaroubaceae

<table>
<thead>
<tr>
<th>Name and molecular formula (1)</th>
<th>Structure (2)</th>
<th>Source (3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Chaparrin (^{80}) (C_{20}H_{28}O_7) (LXXXII)</td>
<td><img src="image1" alt="Structure" /></td>
<td>Quassia</td>
</tr>
<tr>
<td>2. Samaderin (^{81}) (C_{19}H_{22}O_7) (LXXXIII)</td>
<td><img src="image2" alt="Structure" /></td>
<td>Samadera indica</td>
</tr>
<tr>
<td>3. Quassian (^{82}) (C_{22}H_{26}O_6) (LXXXIV)</td>
<td><img src="image3" alt="Structure" /></td>
<td>Quassia amara</td>
</tr>
</tbody>
</table>
Simarouba amara

Besides the degraded members, the triterpenoids with fragment intact have been obtained from members of Meliaceae and Simaroubaceae. These compounds are termed protolimonoids. Some representative members are shown in Table 11.

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)</td>
<td>(2)</td>
<td>(3)</td>
</tr>
<tr>
<td>4. Ailianthone&lt;sup&gt;83&lt;/sup&gt;</td>
<td>Simarouba amara</td>
<td></td>
</tr>
<tr>
<td>( \text{C}<em>{20}\text{H}</em>{24}\text{O}<em>{7}\text{H}</em>{2}\text{O} )</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(LXXXV)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| 5. Galucarubol<sup>79</sup> | Samadra indica |
| \( \text{C}_{20}\text{H}_{28}\text{O}_{8} \) |   |
| (LXXXVI) |   |

Besides the degraded members, the triterpenoids with \( \text{C}_{30} \) fragment intact has been obtained from members of Meliaceae and Simaroubaceae. These compounds are termed protolimonoids. Some representative members are shown in Table 11.
### Table 11: Protolimonoids

<table>
<thead>
<tr>
<th>Name and molecular formula</th>
<th>Structure</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)</td>
<td>(2)</td>
<td>(3)</td>
</tr>
</tbody>
</table>
| **1. Melianol**<sup>84</sup>  
\(C_{30}H_{48}O_{4}\)  
(***LXXXVII***) | ![Structure](image1) | **M. azadirachta** |
| **2. Aphnamaxin**<sup>85</sup>  
\(C_{32}H_{50}O_{5}\)  
(***LXXXVIII***) | ![Structure](image2) | **A. polystachya** |
| **3. Flindissol**<sup>86</sup>  
\(C_{30}H_{48}O_{3}\)  
(***LXXXIX***) | ![Structure](image3) | **Flindersia dissosperma** |
Table 11 (contd.)

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)</td>
<td>(2)</td>
<td>(3)</td>
</tr>
<tr>
<td>4. Malabaricanediol(^{87})</td>
<td>[Chemical Structure]</td>
<td>Ailanthus malabarica DC.</td>
</tr>
<tr>
<td>(\text{C}<em>{30}\text{H}</em>{51}\text{O}_{3})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(XC)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Malabaricol(^{88})</td>
<td>[Chemical Structure]</td>
<td>Ailanthus malabarica DC.</td>
</tr>
<tr>
<td>(\text{C}<em>{30}\text{H}</em>{50}\text{O}_{3})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(XCI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(\text{C}<em>{31}\text{H}</em>{52}\text{O}_{2})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(XCII)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>