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Etagegnehu Assefa
Department of chemistry, College of Natural and Computational Sciences, Wolaita Sodo University, Ethiopia

Amha Admasie
School of Public Health, Wolaita Sodo University, Ethiopia

Corresponding Author:
Etagegnehu Assefa
Department of chemistry, College of Natural and Computational Sciences, Wolaita Sodo University, Ethiopia

Novel natural products from *Taverniera abyssinica* (In Amharic named as Dingetegna)

Etagegnehu Assefa and Amha Admasie

Abstract
Taverniera abyssinica A. Rich, a medicinal plant species belongs to the Fabaceae family commonly known under the Amharic name as dingetegna, literally meaning, remedy against sudden illness. The species is known to occur in Northeast Africa and Southeast Asia. The main objective of this review was to review different literatures regarding the novel natural products from *Taverniera abyssinica* (Dingetegna, in Amharic). The genus *Taverniera abyssinica* is one of among those found in the rural parts of Ethiopia, which are used for the treatment of different diseases such as stomach ulcers, remedy against sudden illness, immediate relief of fever, discomfort and pain, locally as antipyretic and analgesic.

Keywords: Novel natural products and Dingetegna

Introduction
The cultivation and use of spices, herbs, medicinal and other essential oil bearing plants is not new to Ethiopia. It is as old as the crop themselves, and its history can be traced back to the reign of Queen Sheba (ca.992 BC). Ethiopia is the origin and/or center of diversity for many of these plant species. The various literature available show the significant role of medicinal plant in primary health care delivery in Ethiopia where 70% of human and 90% of livestock population depend on traditional medicine similar to many developing countries particularly that of Sub Saharan African countries. The traditional health care is culturally deep rooted with oral and written pharmacopoeias.

Ethiopian plants have shown very effective medicinal value for some ailments of human and domestic animals thus medicinal plants and knowledge of their use provide vital contribution to human and livestock health care needs throughout the country. Such plants include *Phytolacca dodecandra* and many species of *Maytenus*. The major reasons why medicinal plants are demanded in Ethiopia are due to culturally linked traditions, the trust the communities have in the medicinal values of traditional medicine and relatively low cost in using them. The volume of sales of medicinal plants has increased over years and this has been taken by some as the existence of disease prevalence requiring traditional medicare causing increased demand which led to harvesting important medicinal plants. The expected increase in the cost of commercial drugs and their occasional impotency also increase demand of medicinal plants. The proportion of consumers who rely on harvesting medicinal plant is the highest in the rural area, since collecting from natural plantation is most accessible and cost effective.

There are 6500 species of higher plants in Ethiopia making the country one of the most diverse floristic regions in the world. There are large numbers of moderate to high value medicinal plants herbs and spices existing in the wild. It has been widely claimed that about 80% of Ethiopians rely on traditional medicine (predominantly medicinal plants) to treat their illnesses and maintain their health. This is more true in rural than urban areas. Even in urban areas people are inclined to use so-called home remedies to treat common illness symptoms. In such cases, accurate diagnoses of diseases and expertise in preparing and administering herbal medications may not be usually required. In this category of conditions fall such disease states as taeniasis, stomach conditions, skin problems, and symptoms such as headache, cold, cough, and diarrhea. People have treated these conditions for hundreds (maybe even thousands) of years by using traditional ways. They have been successful in most cases in alleviating their suffering by concocting various preparations derived from medicinal herbs which abounded in their environs. More serious medical problems were usually deferred to "expert" traditional medical practitioners, or modern physicians.

Ethiopian traditional medicine consists of various treatment modalities, but the bulk of it employs medicinal plants as part of the treatment regimens. Consistent with the prevailing thoughts of the time, many of the old treatment methods were, as can be expected, steeped in magico-religious beliefs. As time went by, traditional medicine started receiving fresh perspectives. A number of medicinal plants have survived scientific scrutiny to varying degrees.

Taverniera abyssinica A. Rich, a medicinal plant species belongs to the Fabaceae family commonly known under the Amharic name as dingetegna, literally meaning, remedy against sudden illness. The species is known to occur in Northeast Africa and Southeast Asia. It is a threatened medicinal plant that usually grows in a bush land limestone areas with an altitude range of 1700 to 2300 above sea level (Thulin, 1989) [19]. Due to over- exploitation, T. abyssinica is now found as a remnant of isolated and scattered populations in the East Shewa Zone and Tigray region of Ethiopia (Kelbessa E, 1992; Kibebew, *et al.*, 1996; Addis, 2003) [14, 15, 3].

According to ethno-botanical information, *Taverniera abyssinica* has been traditionally used for the treatment of various diseases in Ethiopia. A small bundle of the roots are chewed and the juice swallowed for immediate relief of fever, discomfort and pain. The root extracts are used, locally, as antipyretic and analgesic (Dagne, *et al*., 1990) [5]. Nematicidal and antimicrobial properties have confirmed the rational basis behind the ethno-botanical use of the species (Stadler, *et al*., 1994) [18].

The medicinal importance of T. abyssinica has been recognized by the findings of different chemical compounds isolated from the rootstocks. These chemical compounds include four isoflavonoid derivatives and a new pterocarpan; 3, 4- dihydroxy-9-methoxy therocarpan (Noamesi, *et al*., 1990) [17]. Consequently, pharmacological studies were conducted using rootstock extracts on rats made hypothermic with yeast injection (Dagne, *et al*., 1990) [5]. The aqueous extract of the roots was shown to antagonize the contractile responses of guinea pig ileum to acetylcolin and histamine. At least some of the analgesic properties of the root extracts have been attributed to the isoflavanoids, probably linked to the blocking of histamine receptors (Stadler, *et al*., 1994) [18].

T. abyssinica is one of the ten medicinal plants sold in all the 19 markets surveyed, including the capital city, Addis Ababa (Kloos, *et al*., 1978) [16]. Although the traditional medicinal values (Kloos, *et al.*, 1978; Dagne, *et al*., 1990) [16, 5], the chemical extracts, their effect (Noamesi, *et al*., 1990; Stadler, *et al*., 1994) [17, 18] and the pre- germination treatments of T. abyssinica have been reported, no in vitro regeneration or micropropagation technique has so far been developed for this threatened medicinal plant. Currently, rootstocks of wild T. abyssinica plants are widely harvested for satisfying local markets throughout Ethiopia. Consequently, extensive and uncontrolled exploitation of this species, combined with the decline in natural regeneration, has led to the drastic depletion of the wild species. Although T. abyssinica is a perennial valuable medicinal plant, yet no commercial production under field conditions has been established. Recently, the tissue culture technique i.e. micropropagation has expanded its scope and potential on commercial scale. Micropropagation is suitable for the rapid and large-scale clonal multiplication of elite germplasm. In vitro micropropagation techniques would constitute an approach for the systematic germplasm conservation and genetic improvement. The in vitro regeneration system developed in this research program will rapidly provide large numbers of uniform, pest and disease free plants for investigations of the efficacy of medicinal components in dingatenya and potential commercial production of standard, consistent, and safe preparations.

This species belongs to a small genus, *Taverniera* of Leguminosae family and is found in North East Africa and South West Asia. *Taverniera abyssinica* A. Rich is not known to occur elsewhere and even in Ethiopia it is confined to the provinces of Shoa and Tigray. It is sold in many markets of central Ethiopia under the name 'Dingetegna' literally meaning "medicine for sudden illness", and used for the treatment of headache, stomachache and fever. It is commonly administered by chewing the roots and swallowing the juice (Dagne, *et al*., 1987) [6].

Fig 1: Bundles of 'Dingetegna' bought from market (Photo: Prof. Ermias D., 2010)

Genus Taverniera

The genus Taverniera belongs to the family Fabaceae in the major group Angosperms There are 16 species belongs to the this genus.

Table 1: Different species of Taverniera and the geographical distribution in the world

Species Name	Synonyms	Geographical Distribution
Taverniera abyssinica A.Rich. (Thulin, 1985)	*Taverniera schimperi* Jaub. and Spach var. *oligantha* sensu Cufod	Africa: Ethiopia (Thulin, 1985)
Taverniera aegyptiaca Boiss. (Thulin, 1985)	NA	Africa: Djibouti (Audru *et al*., 1987) Egypt, Ethiopia Sudan Middle East, Saudi Arabia (Thulin, 1985)
Taverniera albida Thulin. (Thulin, 1985)	NA	Asia; Middle East: South Yemen (Thulin, 1985)
Taverniera brevialata Thulin (Thulin, 1985)	NA	Asia; Middle East- Oman (Thulin, 1985)
Taverniera diffusa (Cambess.) Thulin (Thulin, 1985)	*Onobrychis diffusa* Cambess (Thulin, 1985)	Asia- India: Punjab, Rajasthan; Pakistan (Thulin, 1985)
Taverniera echinata Mozaff. (Mozaffarian, 1988)	NA	Asia; Iran (Mozaffarian, 1988)

Species Name	Synonyms	Geographical Distribution
Taverniera glauca Edgew. (Thulin, 1985)	NA	Asia; Middle East: South Yemen (Thulin, 1985); Yemen (Boulos, 1988)
Taverniera lappacea (Forssk.) DC. (Thulin, 1985; Ali, 1977)	*Hedysarum lappaceum* Forssk. (Ali,1977) Tavernicra *stefaninii* Chiov. (Thulin, 1985; Ali, 1977)	Africa: Ethiopia, Somalia, Sudan; Asia (Thulin, 1985) Pakistan (Thulin, 1985; Ali, 1977) Middle East: Oman, Saudi Arabia, South Yemen (Thulin, 1985)
Taverniera longisetosa Thulin	NA	Africa: Somalia (Thulin, 1985)
Taverniera multinoda Thulin	NA	Africa: Somalia; Middle East: Oman (Thulin, 1985)
Taverniera nummularia DC. (Townsend, 1974)	*Taverniera persica* Boiss. and Hausskn.	Asia: Iran (Thulin, 1985; Townsend, 1974; Parsa, 1948; Rechinger, 1984) Iraq (Thulin, 1985; Townsend, 1974; Rechinger, 1984)
Taverniera oligantha (Franch.) Thulin (Thulin, 1985)	*Taverniera schimperi* Jaub. and Spach var. *oligantha* Franch.	Africa: Djibouti (Thulin, 1985)
Taverniera schimperi Jaub. & Spach	NA	Africa: Ethiopia (Thulin, 1985)
Taverniera sericophylla Balf.f.	NA	Africa: Socotra (Thulin, 1985)
Taverniera spartea (Burm.f.) DC. (Thulin, 1985; Ali, 1977; Rechinger, 1984)	*Hedysarum spartium* Burm. F., *Taverniera gonoclada* Jaub. & Spach (Ali, 1977) *Taverniera incana* Boiss. (Thulin, 1985)	Asia; Iran (Thulin, 1985; Parsa, 1948; Rechinger, 1984) Pakistan (Ali, 1977) Middle East: Bahrain, Oman, Qatar, Saudi Arabia, United Arab Emirates (Thulin, 1985)

NA- Not Applicable

Application of Taverniera abyssinica

An antispasmodic (synonym: spasmolytic) is a drug or herb that suppresses muscle spasms. They have been used to treat stomach cramps. Traditionally, they were used to treat stomach ulcers. Most of the drugs used for this purpose as "anticholinergics". The anticholinergic drugs decrease both the movements of the stomach and intestine, and also the secretions of stomach acid and digestive enzymes (htt).

There are two main types of antispasmodic drugs(htt1):

1. Antimuscarinics such as dicycloverine, hyoscine, atropine, propantheline.
2. Smooth muscle relaxants such as aleverine, mebeverine and peppermint oil.

Smooth muscle relaxants are used for smooth muscle contraction, especially in tubular organs of the gastrointestinal tract. The effect is to prevent spasms of the stomach, intestine

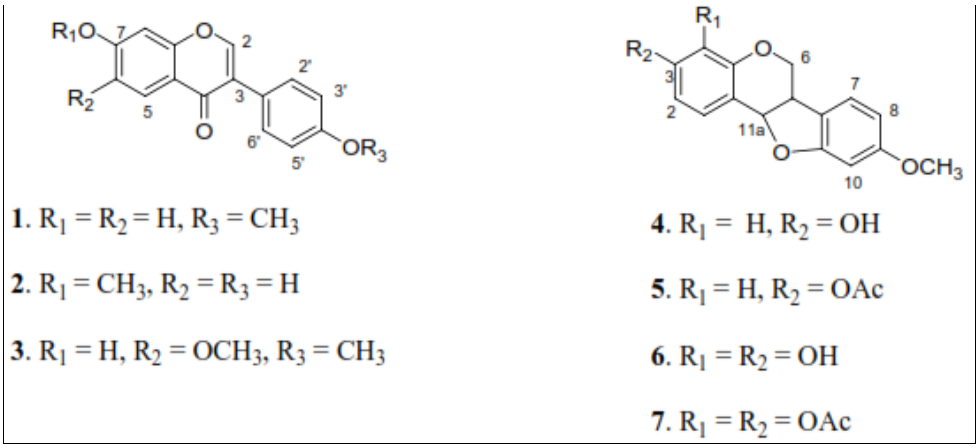
or urinary bladder. Both dicyclomine and hyoscyamine are antispasmodic due to their anticholinergic action.

The traditional analgesic and antipyretic Ethiopian drug "Dingetegna" is made of dried root material of *Taverniera abyssinica A.* Rich (Leguminosae). In a screening for nematicidal natural products, "Dingetegna" extracts showed strong nematicidal activities towards *C. elegans*. In the following, medicarpin and 4-hydroxymedicarpin were isolated as nematicidal constituents from the extracts. In a micro well plate assay for nematicidal activity, both compounds exhibited an LD50 of 25 µg/ml towards *C. elegans*. Beside these nematicidal effects, weak cytotoxic and antimicrobial activities were observed. In addition, both compounds inhibited oxygen consumption of axenically grown *C. elegans*, L 1210 cells, and filamentous fungi. Respiration in sensitive bacteria was not affected. In L1210 cells, the incorporation of precursors into macromolecules was affected in the presence of glucose, indicating that inhibition of respiration is not the only target site of the compounds (Stadler, *et al*., 1994) [18].

Chemistry of Taverniera abyssinica

Previous study on photochemical investigation of *T. abyssinica* (Dagne, *et al*., 1987) entitled with "Isoflavonoids from *T. abyssinica*" has reported the isolation of four compounds which were obtained from different chromatographic separations of petroleum ether as well as chloroform extracts of the roots of the plant. These compounds are classified as isoflavonoids and pterocarpans.

Compounds 1 and 3 were identified as the well known isoflavonoids, formononetin and afromosin, respectively. Compounds 4 and 6 were distinguished as the pterocarpans and they were characterized as medicarpin and 3, 4–dihydroxy–9–methoxypterocarpan, respectively.



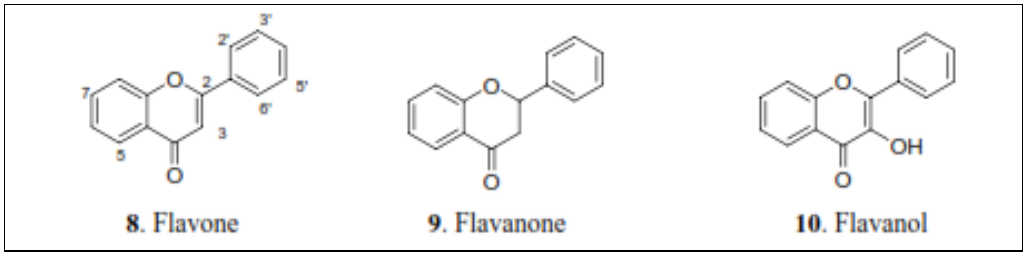
The two compounds isolated from *T. abyssinica*, medicarpin (4), 4-hydroxymedicarpin (6), and also their naturally occurring derivatives found in other plant species have bioactivities such as cytotoxicity activities (Awale, et al., 2008) [4].

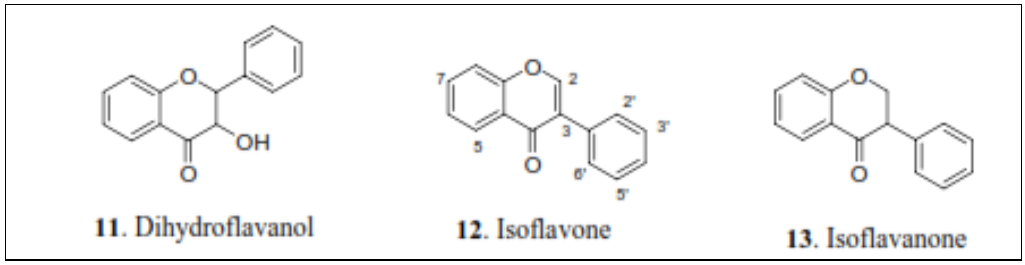
Major Groups of Compounds Isolated from *T. abyssinica*

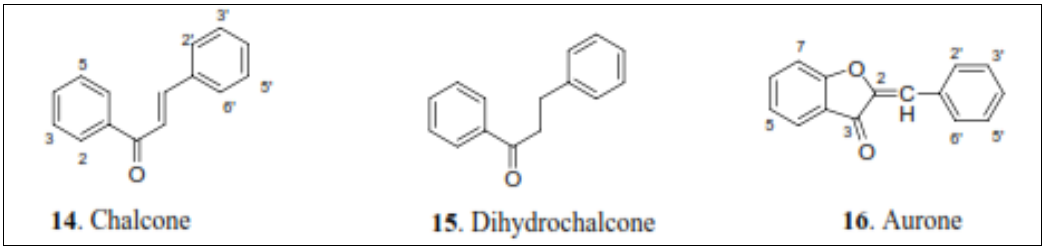
The compounds previously isolated from *T. abyssinica* are classes of natural compounds known as flavonoids. The brief review about flavonoids is presented below.

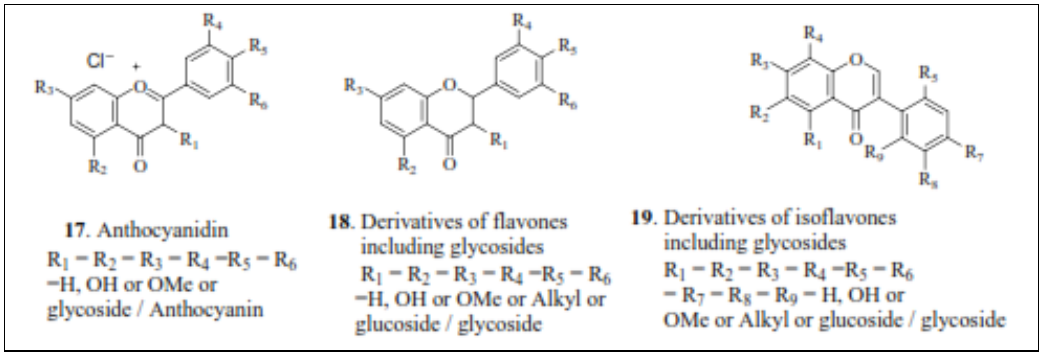
Flavonoids

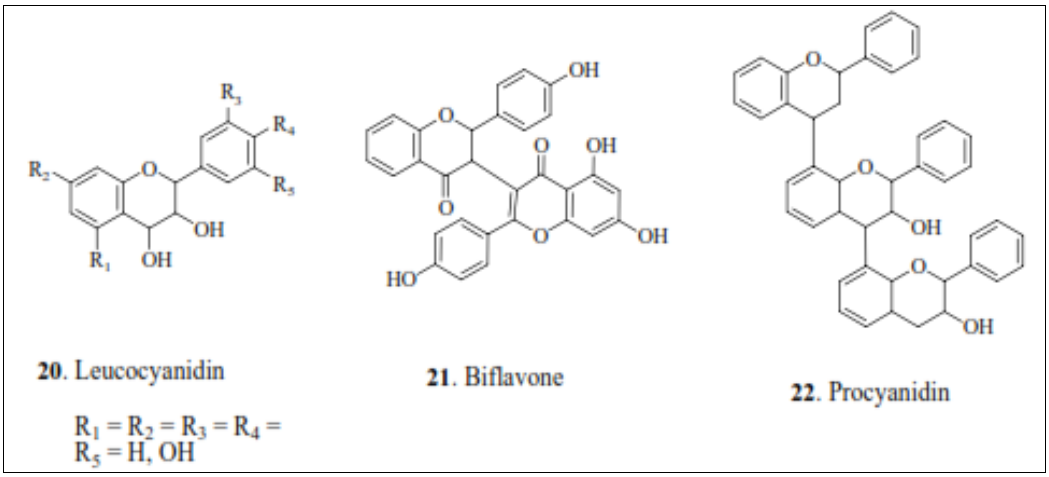
Flavonoids are one of the main groups of natural products. They are a group of naturally occurring phenolic compounds, which occur in different plant parts both in Free State and glycosides. Based on the skeleton of flavonoids some subgroups are: flavones, flavonols, isoflavones, chalcones, aurones. (Fig. 3) (Dewick, 2001) [8].











Isoflavonoids

The isoflavonoids are structural variants of flavonoids in which the Shikimate-derived aromatic ring has migrated to the adjacent carbon of the hetrocycle. The main reason for understanding biosynthesis of isoflavonoids is the fact that some isoflavonoids are produced in plant tissues as stress metabolites or phytoalexins. The isoflavonoids share a common biosynthetic pathway with the flavonoids as far as chalcone – flavanone intermediates, but then a 1, 2–aryl migration (Scheme 2) occurs to produce the rearranged 3-phenylchroman skeleton that differentiates
isoflavonoids from other flavonoids.

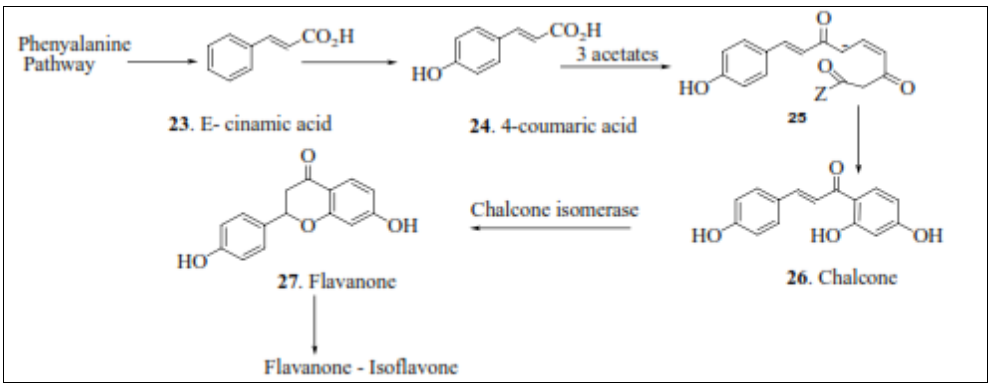
Since pterocarpans are isoflavonoids they share a common biosynthesis pathway of that of flavonoids. The progress of the biosynthesis of flavonoids from primary metabolites can be divided in to a number of phases which are:-

A. Phenylalanine to cinamic acid

An amino acid phenylalanine is used to produce cinamic acid which is a source of the shikimate pathway derived aromatic ring of flavonoids. The enzyme phenylalanine ammonia lyase (PAL) is used.

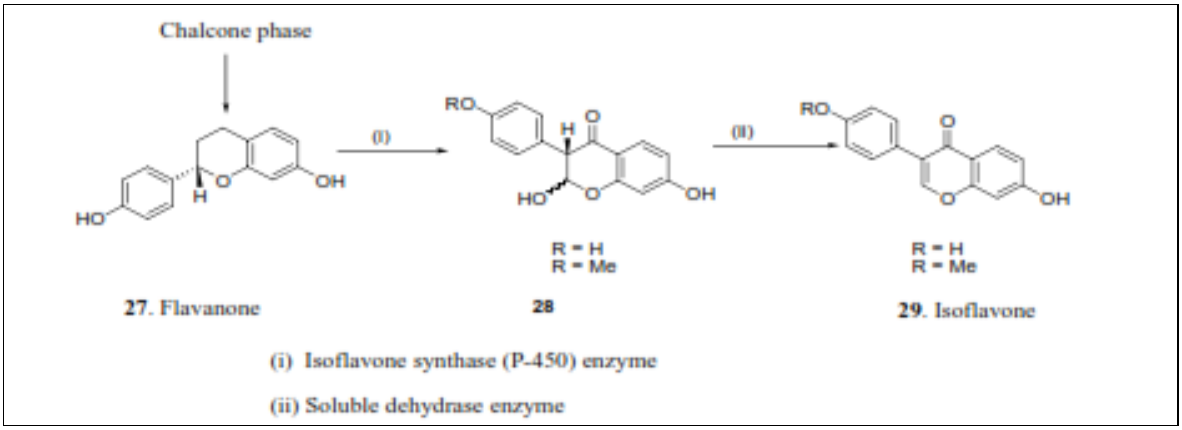
B. The Chalcone – Flavanone Phase

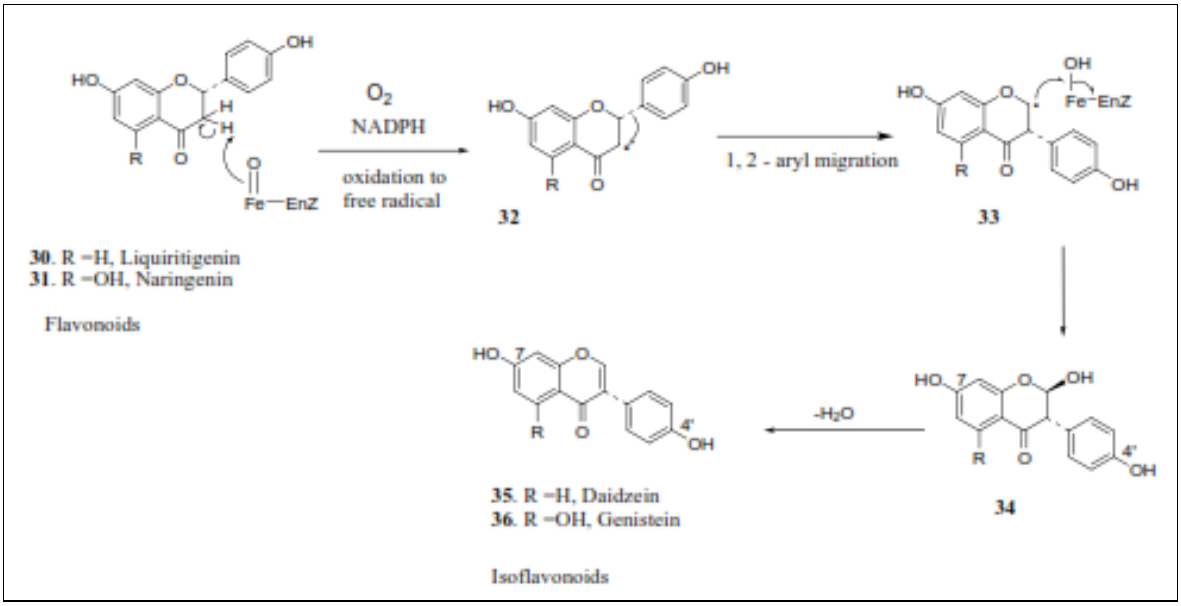
The cinamic acid produced from path A is changed to flavanone through carbon extension.



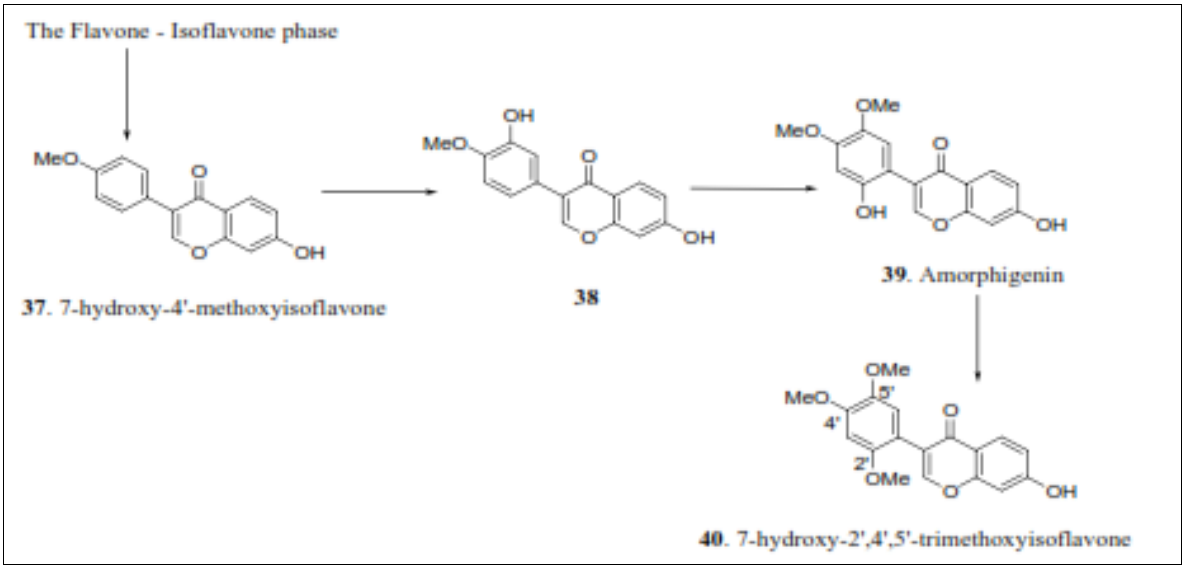
C. The Flavanone - Isoflavone Phase

In this stage the Shikimate-derived aromatic ring has migrated to the adjacent carbon of the hetrocycle. This rearrangement process is brought about by a cytochrome P-450-dependent enzyme requiring NADPH and O *via* intermediate hydroxyisoflavanones. A radical mechanism has been proposed as shown in Scheme 2 below.



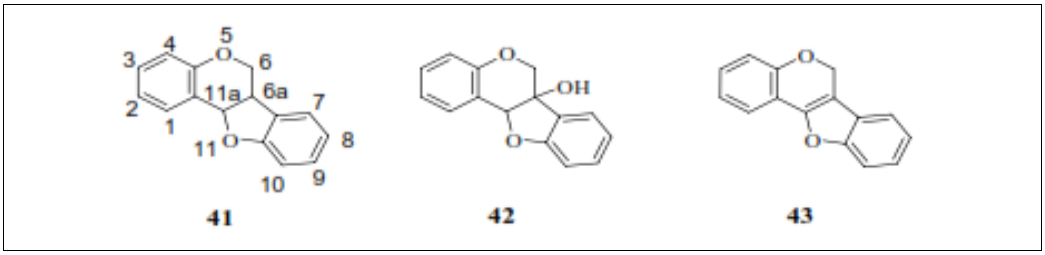


D. The Hydroxylation - Methoxylation Phase

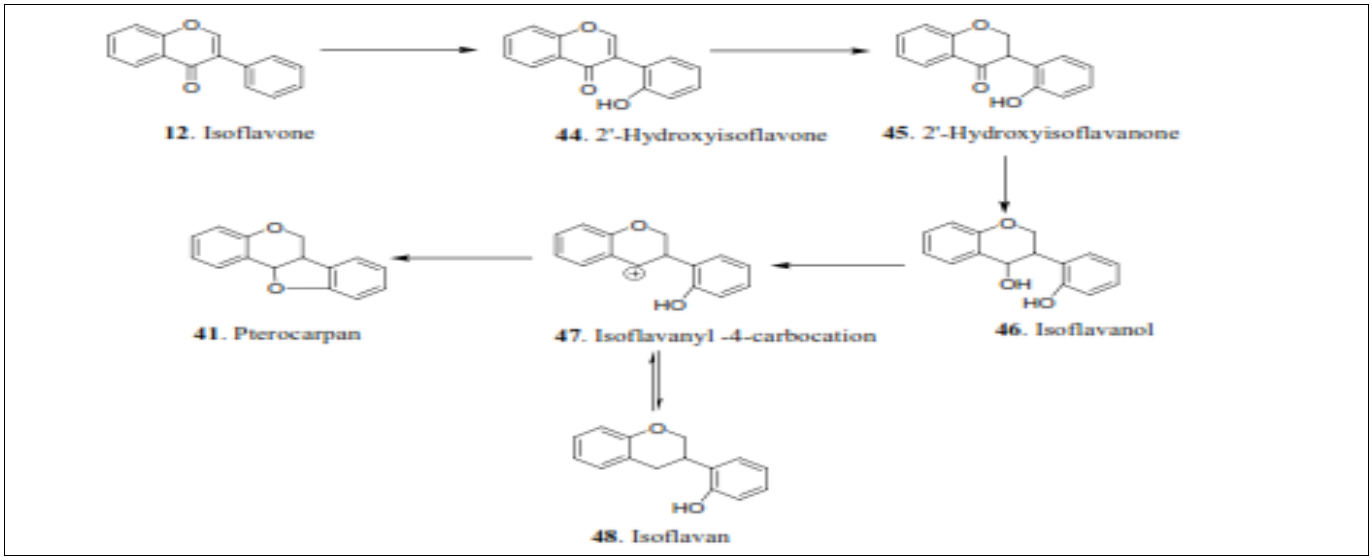


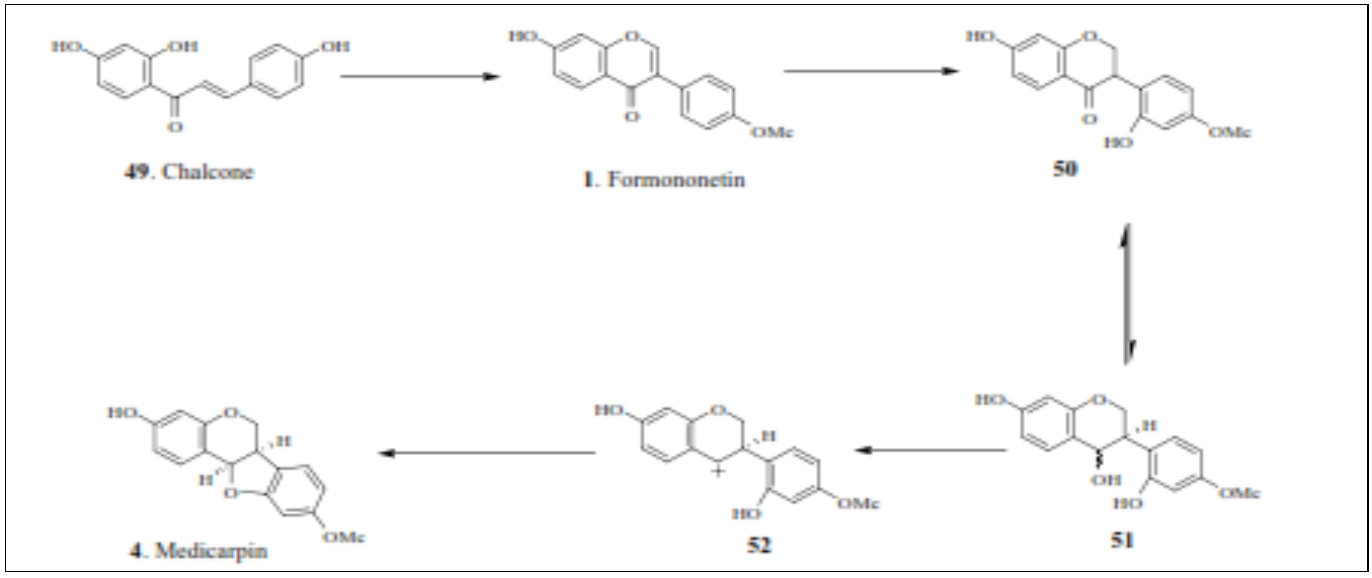
Pterocarpans

Pterocarpans are structural variants of isoflavonoids. They contain a tetracyclic ring system derived from the basic isoflavoinoid skeleton by an ether linkage between the 4 and 2' positions of 12. The systematic numbering shown in structure 41 rather than that for simple isoflavonoids is used. They are the second largest group of isoflavonoids after the isoflavones. Pterocarpans are subdivided in to pterocarpans (41), 6a–hydroxypterocarpans (42) and pterocarpenes (43).



The majority of natural pterocarpans isolated have arisen from phytoalexin studies, using fungal or abiotically stressed plant tissues. Enzymes catalyzing parts of the pathway can be found at much higher levels of activity during the stress period. Scheme 5 shows general pathway of pterocarpan biosynthesis while Scheme 6 presents biosynthesis of a pterocarpan medicarpin from isoflavone formononetin (Harborne, 1988) [13].





Conclusion

Traditional medicine consists of large number of plants with various medicinal and pharmacological importances and hence represents a priceless benefit to the community and the country in reducing high costs in purchasing modern drugs for the treatment of human diseases and livestock health. The genus *Taverniera abyssinica* is one of among those found in the rural parts of Ethiopia, which are used for the treatment of different diseases such as stomach ulcers, remedy against sudden illness, immediate relief of fever, discomfort and pain, locally as antipyretic and analgesic. Nematicidal and antimicrobial properties have confirmed the rational basis behind the ethno-botanical use of the species, sudden illness, and used for the treatment of headache, stomachache and fever, suppresses muscle spasms. Most of the drugs used for this purpose as "anticholinergics". The anticholinergic drugs decrease both the movements of the stomach and intestine, and also the secretions of stomach acid and digestive enzymes.

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