The Compositae (Asteraceae) family is nested high in the Angiosperm phylogeny in Asterideae/Asterales. The family contains the largest number of described, accepted, species of any plant family, ca. 24,000, with estimates of the total number reaching 30,000. There are 1600-1700 genera distributed around the globe except for Antarctica (Funk *et al.*, 2009). Economically, plants of the family Compositae are of considerable importance. Some are food plants (e.g. *Helianthus annuus*, *Lactuca sativa*, *Cichorium* spp., *Cynara scolymus*) and others are drug plants (e.g. *Artemisia* spp., *Matricaria chamomilla*, *Chrysanthemum cinerariaefolium*). On the other hand, many are ornamentals (e.g. *Aster* spp., *Helianthus* spp.) and several are noxious weeds (e.g. *Senecio* spp.). From the medical point of view, many of the plants are used in medicine and some are pharmacopoeial drugs, e.g. *Artemisia cina*, *Calendula officinalis* and *Matricaria chamomilla*, etc. (Trease, 1966). Moreover, many of the plants are used in folk medicine as herbal remedies, e.g. *Artemisia* spp. and *Achillea millefolium*.

Constituents

Plants of the Compositae store mainly proteins and oils in their seeds. As a rule, the seed oils are rich in linoleic acid and contain lesser amounts of oleic and palmitic acid; linolenic and stearic acid are minor fatty acids. The family may be designated as a group with the linoleic-rich variant of seed oils of the usual type. It has been reported that seeds of many Compositae contain unusual fatty acids besides or replacing linoleic acid and that the chemistry of seed oils is often characteristic of taxa (Hegnauer, 1977).

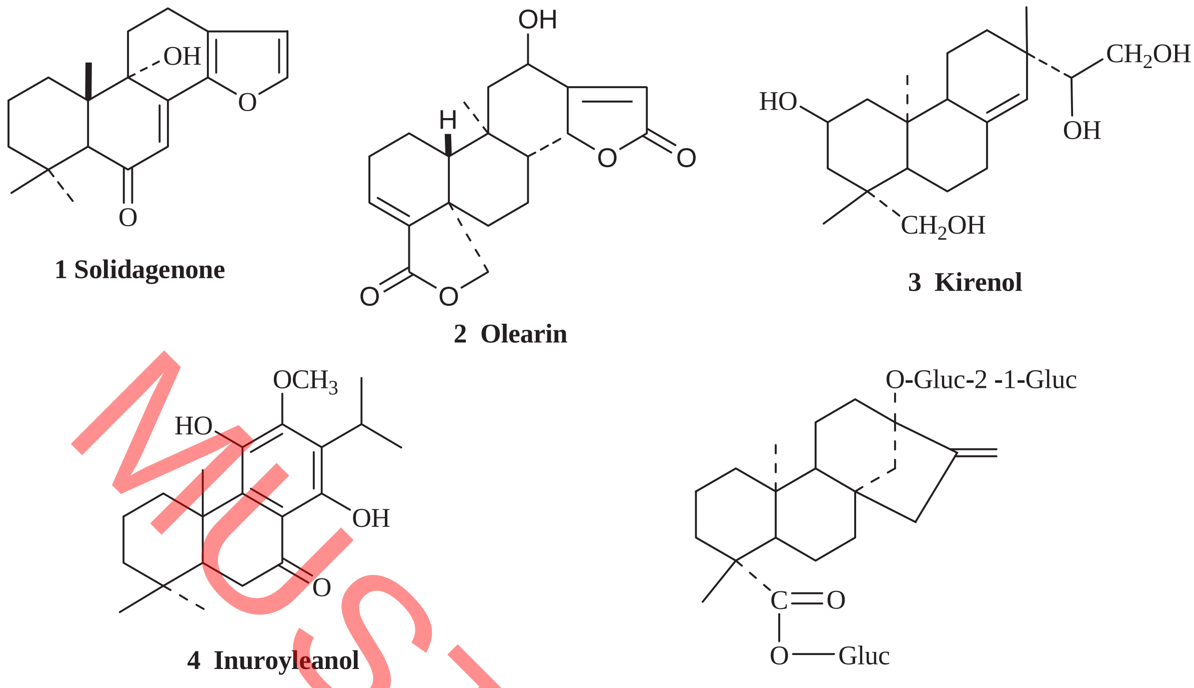
The main secondary metabolites isolated from the species of Asteraceae are monoterpenes, sesquiterpenes, sesquiterpene lactones, diterpenoids, triterpenoids, polyacetylenes, flavonoids, benzofurans, benzopyrans and coumarins. All of the classes currently have a number of representatives (at least several hundreds) that are considered to be satisfactory for studying the chemotaxonomy (Scotti *et al.*, 2012).

The combined occurrence of sesquiterpene lactones, acetylenic compounds and inulin type fructans is almost as characteristic of the Compositae as are their head like inflorescences (capitula). Triterpenes and flavonoids are present in every member of the family and some of their structural features suggest family specific trends with regard to triterpene and flavonoid synthesis (Hegnauer, 1977). Inulin-type fructans probably occur in all composites except a few annual species (Hegnauer, 1964).

- Sesquiterpene lactones: The main active principle of the majority of the drug plants are bitter principles besides the volatile oil. These bitter substances are of the sesquiterpene lactone type, a class of compounds almost unique in this family. Mabry and Bohlmann (1977) reported that over 90% of the more than 600 known sesquiterpene lactones belong to the Compositae. Various dicotyledonous families produce simple germacrane-derived sesquiterpene lactones, but only the Asteraceae (Compositae) is characterized by an array of structurally modified and highly substituted compounds. Till 1982, over 1300 different structures have been isolated from members of all but two of the family's 15 tribes (Seaman, 1982). The distribution of sesquiterpene lactones within Compositae appears to harmonize at least partially with the divisions laid down by classical plant taxonomy, especially when attention is paid to those structural features that involve alterations in the carbon skeleton

(Herz, 1977). By far the largest number, typical of Compositae, are γ-lactones. The distribution of the various sesquiterpene lactones in the tribes of Compositae has been examined and/or reviewed by several workers (e.g. Hegnauer, 1977; Herz, 1977; Ciccio *et al.*, 1978; Seaman, 1982; Scotti *et al.*, 2012). They occur in all tribes. However, variations within species and genera render these constituents suitable for taxonomic studies at specific and sectional levels and for the study of speciation and plant migration (Hegnauer, 1977). Ainsliatrimers A and B, two guaianolide-type sesquiterpene lactone trimers, together with one structurally related sesquiterpene dimer ainsliadimer B, were isolated from the aerial part of *Ainsliaea fulvioides* H. Chuang (Wang *et al.*, 2008a).

- Diterpenes and triterpenes: Compositae plants are triterpene accumulators. Monols and diols of the oleanol, ursanol and lupeol type are most characteristic of the family. They occur free or, more frequently, esterified with acetic acid or fatty acids in the lipid fractions of roots, stems, flowers and fruits and, in *Cichorieae*, in lattices (Hegnauer, 1964, 1977). β-Amyrin, taraxerol, germanicol, α-amyrin, taraxasterol, pseudotaraxasterol and lupeol have been isolated from many members of the family. Taraxerol, germanicol, taraxasterol and pseudo-taraxasterol are somewhat typical constituents. The presence of several diols (e.g. faradiol, calenduladiol, erythrodiol) has also been reported (Hegnauer, 1977). Oleanolic acid and its derivatives (e.g. echinocystic acid) are the main sapogenins of saponin-accumulating taxa of the family (e.g. *Calendula*, *Helianthus*, etc.) (Hegnauer, 1977). Hegauer (1977) reported that so far, known diterpenoids of the family belong to four main classes: bicyclic, tricyclic, tetracyclic and pentacyclic diterpenoids. They are more or less common in some tribes (*Astereae*, *Calenduleae*) and extremely rare or totally lacking in others (e.g. *Cyanareae*, *Cichorieae*). Diterpenoids occur in Compositae, free, esterified or glycosylated depending on the taxa concerned and on the plant parts where accumulation takes place. Several types of diterepenes were identified including clerodanes e.g. amphiacrolides A-E from *Amphiachyris dracunculoides* (Harraz and Doskotch, 1990), 12-*epi*-bacchotricuneatin A from *Laennecia sophiifolia* (Simirgiotis *et al.*, 2000), *ent*-pimarane diterpenes from *Palafoxia texana* (González *et al.*, 1990), labdane diterpenes [e.g. 8α-hydroxylabd-14(15)-ene-13(*S*)-*O*-β-D-ribopyranoside,13-hydroxy-7-oxolabda-8,14-diene 13(*R*)-*O*-α-L-arabino-pyranosideand 13-hydroxy labda-7,14-diene 13(*R*)-*O*-α-L-arabinopyranoside] from *Egletes viscosa* (Lee *et al.*, 2005a; Artur e Silva-Filho *et al.*, 2007) and *ent*-kauranoids e.g. *ent*-kaur-16-en-19-oic acid from *Cacalia pilgeriana* (Li *et al.*, 2007). Other examples of the diterpenoids of Compositae are solidagenone (**1**), olearin (**2**) from the *Astereae*, kirenol (**3**) from *Heliantheae*, inuroyleanol (**4**) from *Inuleae* and stevioside (**5**), an extremely sweet-tasting glycoside from *Eupatorieae* (**Fig 1)** (Hegnauer, 1977).

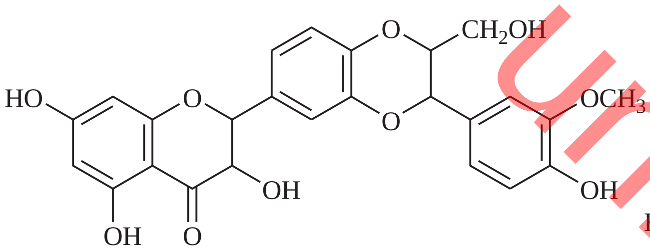


1 Solidagenone **2 Olearin** **3 Kirenol** **4 Inuroyleanol** **5 Stevioside**

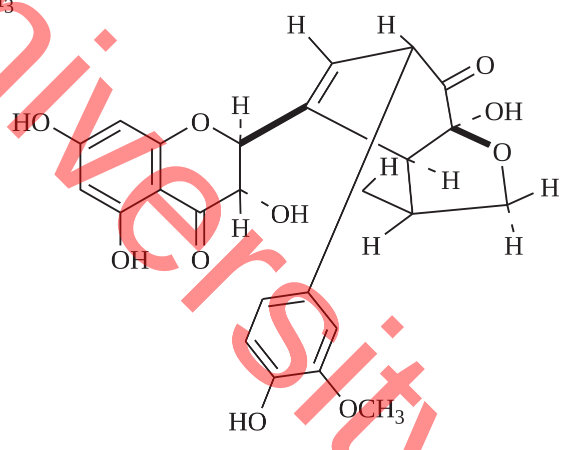
Fig. 1

- Flavonoids: The Compositae is rich with flavonoids (Harborne, 1977), particularly methylated ethers (Rodriquez *et al*., 1972; Harborne *et al*., 1976; Rizk, 1986). The family is also characterized by the frequent occurrence of 6-hydroxylated compounds, e.g. quercetagetin (6-hydroxyquercetin), scutellarein (6-hydroxyapigenin) and 6-hydroxyluteolin where they are represented by several of their glycosides. The common flavonols kaempferol and quercetin and the common flavones apigenin and luteolin have been reported to be widely distributed in this family. Bate-Smith (1962) recorded quercetin in 64%, and kaempferol in 56% of the species he surveyed. Members of several genera of Asteraceae, belonging to the tribes *Mutisieae*, *Cardueae*, *Lactuceae* (all subfamily Cichorioideae), and of *Astereae*, *Senecioneae*, *Helenieae* and *Heliantheae* (all subfamily Asteroideae) have been analyzed for chemodiversity of their exudate flavonoid profiles. Investigation of the exudate flavonoids of a series of Asteraceae, belonging to the tribes Astereae, Eupatorieae, Helenieae and Heliantheae, revealed that methyl ethers of apigenin, luteolin, kaempferol, and quercetin as well as methyl ethers of their relevant 6 -hydroxy derivatives were abundant, whereas 8-*O*-substituted derivatives and flavanones were encountered only occasionally; 6,8-di-*O*-substituted flavonols were found in only one species (Wollenweber *et al.* 1997). The majority of structures found were flavones and flavonols, some times with 6- and/or 8-substitution, and with a varying degree of oxidation and methylation. Flavanones were observed in exudates of some genera, and, in some cases, also flavonol- and flavone glycosides were detected (Valant-Vetschera and Wollenweber, 2007). The relatively frequent occurrence of chalcone glycosides (the flower pigments of several genera, e.g. *Bidens*, *Cartharmus* and *Helichrysum*) where they are often accompanied by the corresponding aurones (Farkas and Pallos, 1967) or flavonones have been also reported (Hegnauer, 1977).

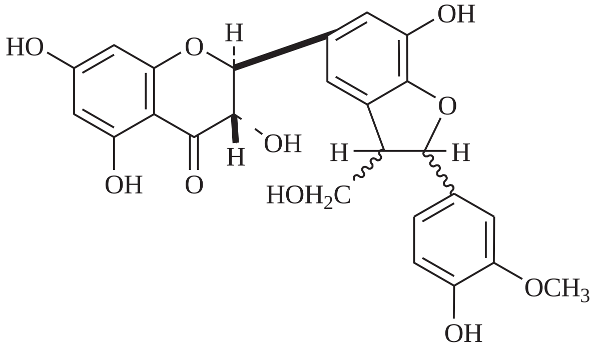
In general, flavonoids have been shown to be good taxonomic markers for Asteraceae. More than 800 compounds comprising 4700 flavonoid occurrences were included in a computational system. Some implications of flavonols, flavones and other types as well as structural features of them are discussed for tribes and subtribes of Asteraceae (Emerenciano *et al.* 2001). Unusual flavonoids in the family include the flavonolignans of *Silybum marianum*, e.g. silybin **(1),** silydianin **(2)** and silychristin **(3)** (Haensel *et al.*, 1972; Wagner, 1977), the *Helichrysum* flower pigment (obtusifolin, **4)** **(Fig 2)** (Haensel *et al.*, 1970) and the isoflavonoids wedelolactone (from *Eclipta*, *Wedalia*), demethylwedelolactone and its 7-glucoside (*Wedalia*) (Bhargava *et al.*, 1972). The rare flavone isoetin (5,7,2',4',5'- pentahydroxyflavone has been identified as a yellow flower pigment in *Cichorieae* (Harborne, 1978). Reviews dealing with the distribution of anthocyanins, flavonoids and related compounds in the family have been given (e.g. Harborne, 1977; Hegnauer, 1977). Yellow anthochlor pigments (two interrelated structural types: chalcones and aurones) are of limited distribution in composite flowers; they occur regularly in only one group of related taxa centred about *Bidens*, *Coreopsis* and *Dahlia* (Hegnauer, 1977).



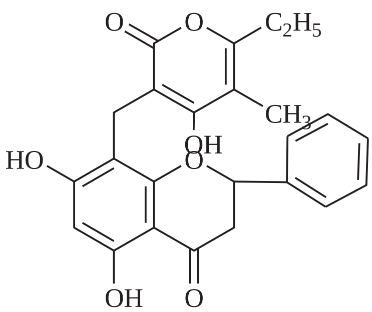
1 Silybin



2 Silydianin



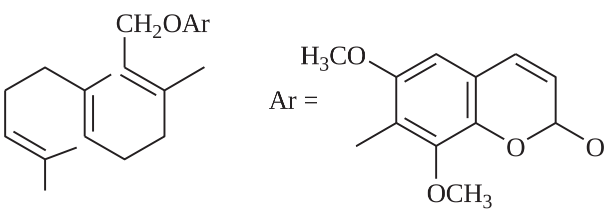
3 Silychristin



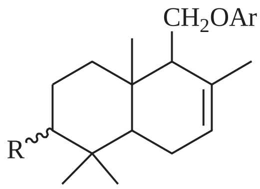
4 Obtusifolin

Fig. 2

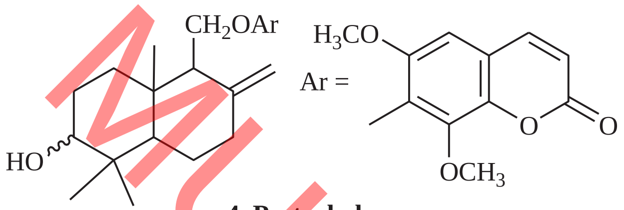
- Other Phenolics: Coumarins have been reported as constituents of a number of species representing several tribes. They occur both as free or glucosides. The presence of coumarins in the seeds of eighty-one species from forty-five genera has been recorded by Kaminski *et al.* (1979). Sesquiterpene-coumarin ethers (e.g. **1-4)** have been identified from *Achillea* and *Artemisia* spp. Simple phenolics, e.g. hydroquinone, arbutin **(5)** and picein **(6)** have been identified from the family. Caffeic acid represents one of the major phenolics of Compositae, which is usually present as a mixture of chlorogenic acids including cynarin **(7)** and sometimes as cichoric acid. Fukinolic acid (**8**), fukiic acid (**9**) as well as several others have been also isolated from plants belonging to the different tribes of the family (Hegnauer, 1977; Rizk, 1986). An extremely varied array of chromenes and benzofurans has been reported to occur in some tribes of the Compositae, e.g. ageratochromene (**10**), euparin (**11**) in *Eupatoriae*; tremetone (**12**) and hydroxytremetone (**13**) in *Astereae*, stoebenone (**14**) in *Inuleae*, and encecalin (**15**) and espeletone (**16**) (**Fig 3a)** in *Heliantheae* (Hegnauer, 1977). Several isobutyric and isovaleric esters (of the dihydrobenzofuran type compounds) have been isolated from the *Senecioneae*. Phthalides and α-pyrones were reported to occur in the *Inuleae* and *Senecioneae*, e.g. the phthalides (**17-19**) and helipyrone (**20**), arenol (**21**) and homoarenol (**22**) (**Fig 3b)** in *Helichrysum* spp. (Rizk, 1986). Three dimeric benzofuran derivatives, ligulacephalins A, Band C, were isolated from the roots of *Ligularia stenocephala* Matsum. et Koidz. together with 5,6-dimethoxy-2-isopropenyl-benzofuran, euparin and (*R*)-(-)-hydroxytremetone (Toyoda *et al.*, 2005). The isolation of benzofurans from several other species was reported e.g. *Gerbera saxatilis* (Chen *et al.*, 2007). Lignans were identified from some species e.g. lappaol F, lappaol H (Ichihara *et al.*, 1978), neoarctin A from *Arctium lappa* (Wang and Yang, 1995), saussol from *Saussurea hieracioides* (Liu *et al.*, 1989) and vladinols A-F from *Vladimiria souliei* (Tan *et al.*, 1990).
- Acetylenes: Acetylenes have been detected in most organs of the Compositae. However, the root usually being the richest source and very often they can be isolated from this plant part. Acetylenic compounds have been isolated from all the twelve tribes which constitute the sub-family Tubliforae (Swain, 1963; Bohlmann *et al.*, 1973). Apart from three exceptions from other plant families, the Compositae is unique in containing some twenty-six cyclic or heterocyclic structural elements derived from acetylenic precursors and some four to five other heterocycles where formation from acetylenes is unlikely (Sorensen, 1977). Lachnophyllum ester isolated from *Lachnophyllum gossypinum* (*Astereae*) was the first diacetylenic compound with established constitution. Compounds with extended unsaturation are more common in the tribes *Astereae* and *Anthemideae* than lachnophyllum ester (Sorensen, 1977). One of the polyacetylenes often found in most of the remaining composite tribes is the pentaacetylene (tridecapentayenene), which has been found in ten out of the thirteen tribes. The thiophene derivatives of the Compositae, a very large group originate from two acetylenic bonds and hydrogen sulphide. Bohlmann *et al.* (1973) isolated the thiophenes which are clear-cut analogues of a compound which could not be isolated by the usual isolation techniques. Thiophenes are widely distributed in the family (Sorensen, 1977).



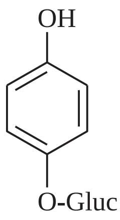
1 Farnochrol



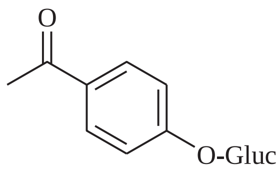
2 Dimartol A:R = OH ax
3 Dimartol B:R = OH eq



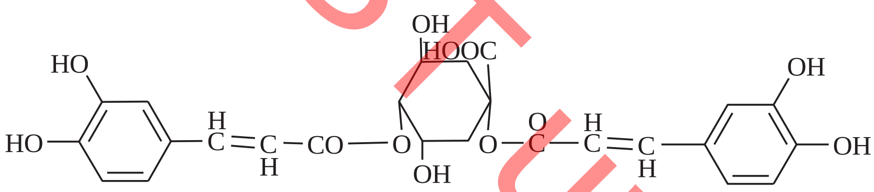
4 Pectachol



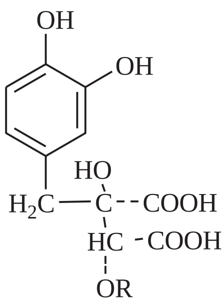
5 Arbutin



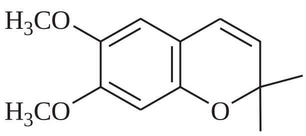
6 Picein



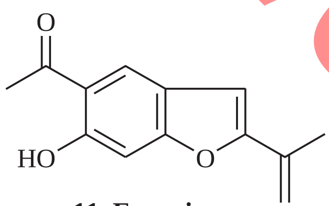
7 Cynarin



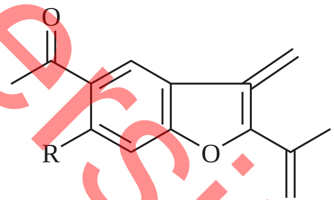
8 Fukinolic acid: R=Caffeyl-
9 Fukiic acid: R= H



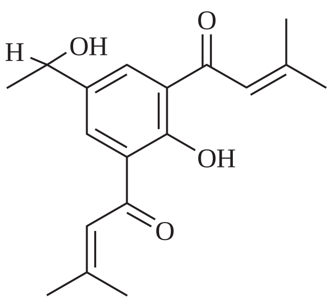
10 Ageratochromene



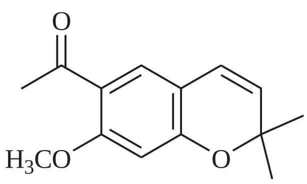
11 Euparin



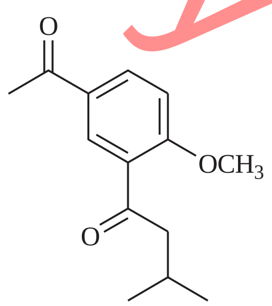
12 Tremetone :R=H
13 Hydroxytremetone :R=OH



14 Stoebenone

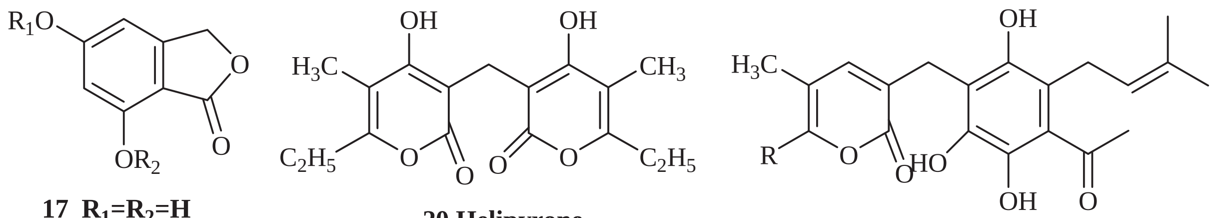


15 Encecalin



16 Espeletone

Fig. 3a



17 R_1=R_2=H
18 R_1=R_2=CH_3
19 R_1=CH_3; R_2=H

20 Helipyrone

21 Arenol : R=CH_3
22 Homoarenol : R=C_2H_5

Fig. 3b

Reviews about the distribution of acetylenes in Compositae and their use as a tool for chemotaxonomical studies and classification within the family have been given by several scientists (Swain, 1963; Sorensen, 1977; Bohlmann *et al.*, 1973; Konovalov, 1996). The chemical investigations of several *Achillea* spp. have shown that acetylenic compounds with an amide grouping are characteristic for this genus (e.g. Bohlmann and Zdero, 1973; Greger *et al.*, 1981). These compounds have also been isolated from members of other genera (e.g. *Anacyclus* and *Leucocyclus* (Bohlmann *et al.*, 1973; Greger *et al.*, 1981). Many of these amides are piperidides and pyrrolidides (Greger *et al.*, 1982, Rizk, 1986).

- Essential Oils: Many of the plants of the Compositae are aromatic plants and yield appreciable amounts of essential oils. Volatile constituents are mainly monoterpenoids and sesquiterpenoids. The phenolic monoterpenoid thymol and a large number of thymol derivatives, both free and esterified are common constituents of certain taxa of the tribes *Eupatorieae*, *Inuleae* and *Helenieae* (Hegnauer, 1977). Irregular monoterpenoids having the artimesyl, santolinyl or chrysanthemyl skelton have been also identified from Asteraceae (Epstein and Poulter, 1973). Furanosesquiterpenes (e.g. 12-acetoxy-10,11-deydrongaione) have been isolated from several species (Rizk, 1986).
- Alkaloids: Alkaloids have been isolated from many plants of the family. Plants belonging to the tribe *Senecioneae* and *Eupatorieae* are among plants known to contain pyrrolizidine alkaloids which occur as both tertiary bases and *N*-oxides. Pyrrolizidine alkaloids seem to be more or less universal in *Senecioneae* and may be considered as one of their outstanding biochemical features. Moreover, *Heliantheae* (*Eclipta*, *Zinnia*) synthesizing nicotine, nornicotine and anabasine and the echinopsine-producing genus *Echinops* (*Cardueae*) can all be mentioned as taxa with well-characterized alkaloids. From other taxa, alkaloid-like substances such as diterpene alkaloids from *Inula royleana* (*Inuleae*) and betaines e.g. betaine, trigonelline, chrysanthemine (= stachydrine) have been reported (Hegnauer, 1977; Rizk, 1986). In general, the Compositae was considered as a group in which alkaloids are not rare. At the same time available evidence suggested that alkaloid patterns are characteristic of species, genera or tribes rather than of the family as a whole (Hegnauer, 1977).
- Other (miscellaneous) constituents: The presence of several other compounds in the family has been reported. The cyclohexanehexol, L-inositol, is known from twelve

species belonging to eleven genera and seven tribes. Scyllitol, too, was found by Plouvier (1971a,b, 1972) to occur widely in Compositae; he isolated it from sixty-one species belonging to genera representing all tribes of the family. The presence of other cyclitols (e.g. L-viburnitol, L-quercetol, L-leucanthenitol, L-pinitol) in several species has been reported (Rizk, 1986). According to Hegnauer (1977), the accumulation of inulin-type fructans and the isomeric cyclitols linositol and scyllitol together form a very distinct feature of the family. Isobutyl amides of long-chain fatty acids with characteristic olefinic and acetylenic unsaturation patterns were known from members of *Anthemideae* and *Heliantheae*. Examples of these constituents (which usually have a pungent taste and possess insecticidal properties) are pellitorin, scabrin and echinacein (Hegnauer, 1977). Phytoecdysteroids were isolated from some species e.*g*. rhapontisterone (Guo *et al*., 1991), ecdysterone, ajugasterone C, ajugasterone C 20,22 monoacetonide, 2,3,20,22-diacetonide ajugasterone (Zhang *et al*., 2002a) from *Rhaponticum uniflorum*, carthamosterones A and B from *Rhaponticum carthamoides* (Ramazanov *et al*., 1997a,b), lesterone, rhapisterone from *Leuzea carthamoides* (Borovikova and Baltaev, 1999; Borovikova *et al*., 1999), 20-hydroxyecdysone, integristerone A, 2-deoxy-20-hydroxyecdysone from *Serratula komarovii* (Vorob′eva *et al*., 2004) and others (Vokáč *et al*., 2002). Cyanogenic plants are known from several tribes of Compositae (Hegnauer, 1977; Fikenscher *et al*., 1980). Examples of the cyanophoric constituents identified from the family are amygdalin, linamarin and lotaustralin (Rizk, 1986). From the fruits of *Xeranthemum cylindraceum*, *Cardueae*, five cyanogenic glycosides [sambunigrin, zierin, epilucumin, zierinxyloside and xeranthin (acylated trisaccharide)] have been identified (Schwind *et al*., 1990).

The family is represented in Egypt by 98 genera and 234 species (Bolous, 2009).

32.1 *ACHILLEA* L.

Many components which are highly bioactive have been isolated from *Achillea* species. The first natural proazulene, identified from the genus *Achillea*, achillicin (**1**) was isolated from *Achillea millefolium* (Banh-Nhu *et al*., 1979). Reviews of phytochemical constituents of *Achillea* species (Si *et al*., 2006; Saeidnia *et al*., 2011) revealed the identification of the following classes of compounds: flavonoids [e.g. luteolin (**2**), cynaroside (**3**), apigenin (**4**), cosmosiin (**5**), centaureidin (**6**), quercetin (**7**), salvigenin (**8**), galangin (**9**), and eupatilin (**10**)], sesquiterpene lactones, other terpenoids, lignans [e.g. epiaschantin (**11**), aschantin (**12**), episesartemin (**13**), sesartemin (**14**), epieudesmin (**15**), epiyangambin (**16**), yangambin (**17**) and others] from *Achillea holosericea* (Ahmed *et al*., 2002a), amino acid derivatives, fatty acids, alkamides [e.g. *p*-hydroxyphenethylamide (**18**)] (**Fig. 4**) and a few other types of compounds (fatty acids, alkanes, and inulin). A sequiterpene lactone, containing chlorine was isolated from *Achillea ligustica* (Hegazy *et al*., 2008). The genus *Achillea* comprises flavored species which produce intense essential oils. A large number of components (149 compounds) were found in the oils of *Achillea millefolium*, *Achillea pannonica* and *Achillea collina*. The monoterpenes, 1,8-cineole,