■ **CHAPTER - I**

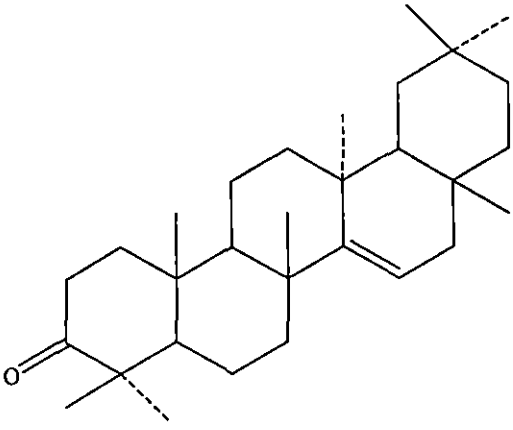
REVIEW OF LITERATURE

At the onset of the present study, it was considered worth while to review the work of the previous workers regarding triterpenoids in a selective manner. The observations of the previous workers have been presented briefly in the following paragraphs. For convenience, the observations have been divided into two subgroups which are as follows:

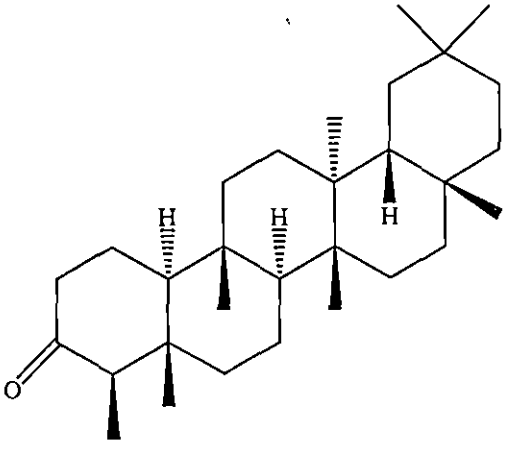
1. **Phytochemical investigations on medicinal plants containing triterpenoids as major constituents.**
2. **Potential antimicrobial activities of triterpenoids and their derivatives.**

1. Phytochemical investigation on medicinal plants containing Triterpenoids as major constituents

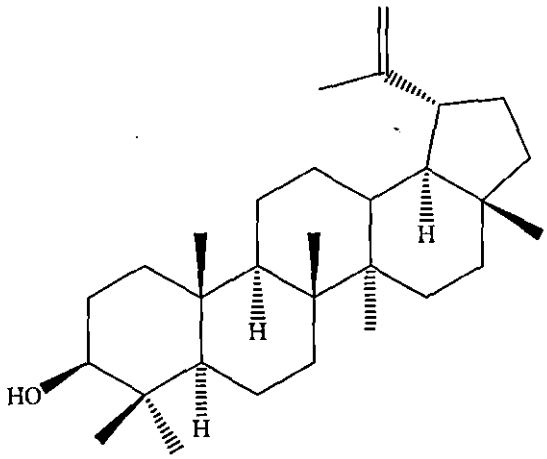
Gunaskera *et al.*[11] isolated new lupane derivative 3β–hydroxy-28-*p*-coumaroyloxy-lup-20(29)-27-oic acid from *Caesalpia densifolia* and whose structure was deduced by chemical correlation with betulin, Simiarenol, taraxerone, friedelin, lupeol, betulinic acid, betulin, and β-sitosterol-g-D-glucoside.



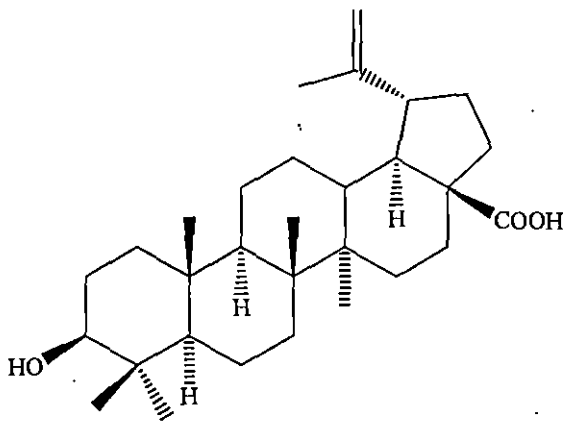
Taraxerone (1)



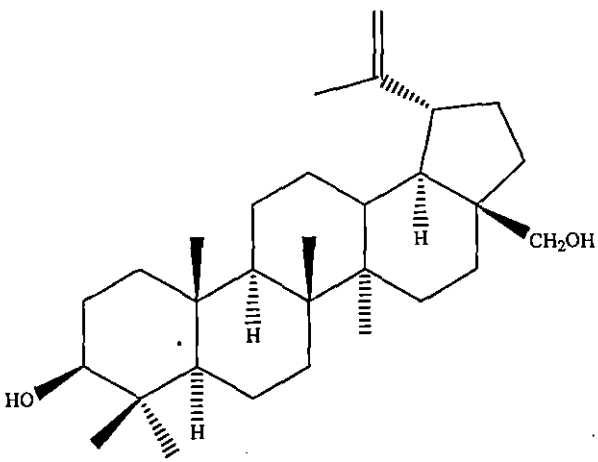
Friedelin (2)



Lupeol (3)

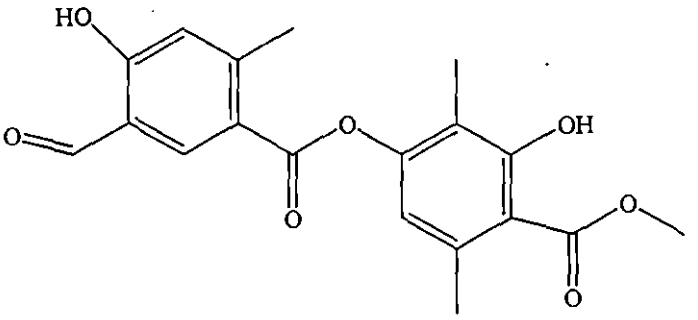


Betulinic acid (4)

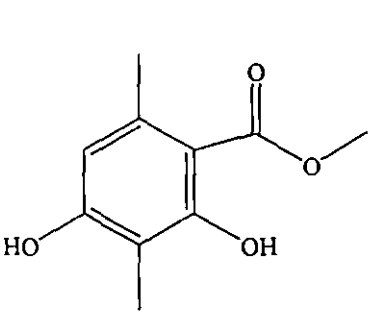


Betulin (5)

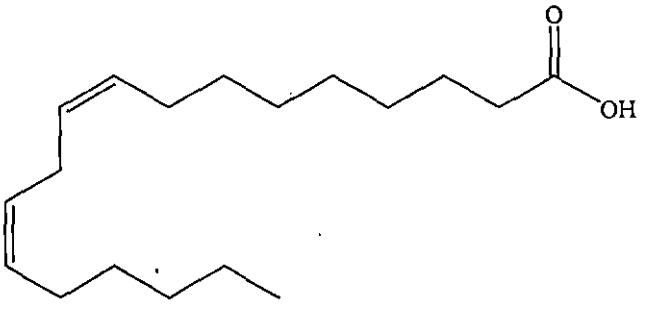
Mutai *et al.*[2] isolated three new pentacyclic triterpenoids: (20R)-3-oxolupan-30-al, (20*S*)-3-oxolupan-30-al and (20*R*)-28-hydroxylupen-30-al-3-one, along with (20*S*)-3β-hydroxylupan-30-al and the known metabolites 30-hydroxylup-20-(29)-en-3-one, 30-hydroxylup-20-(29)-en-3β-ol, atranorin, methyl2,4-dihydroxy-3,6-dimethylbenzoate, sitosterol-3β-O-glucoside and linoleic acid from *Acacia mellifera* . The structures of the new metabolites were elucidated by extensive spectroscopic analyses and their relative stereochemistry was determined by NOESY experiments. They observed that the new metabolite 3 exhibited significant cytotoxic activity against the NSCLC-N6 cell line, derived from a human non-small-cell bronchopulmonary carcinoma.



Atranorin (6)

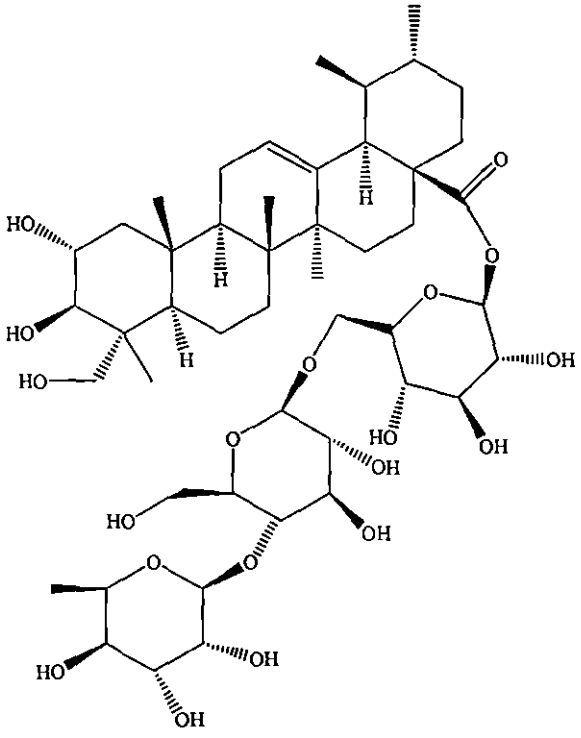


Methy-l2,4-dihydroxy-3,6-dimethylbenzoate (7)

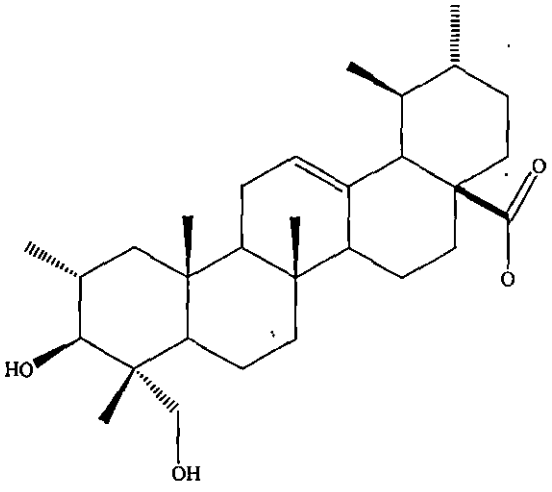


Linoleicacid (8)

James and Dubery[3] accumulated large quantities of pentacyclic triterpenoid saponins collectively known as centelloids from *Centella asiatica*. These terpenoids include asiaticoside, centelloside, madecassoside, brahmoside, brahminoside, thankuniside, sceffoleoside, centellose, asiatic-, brahmic-, centellic- and madecassic acids. They studied biological activity of these compounds, the Centella triterpenoids can be regarded as phytoanticipins due to their antimicrobial activities and protective role against attempted pathogen infections. They reported that these plant-derived pharmacologically active compounds have complex structures; the production of secondary metabolites by cultured cell provided a particular important benefit of manipulation and improved the production of the desired compounds.



Asiaticoside (9)



Asiatic acid(10)

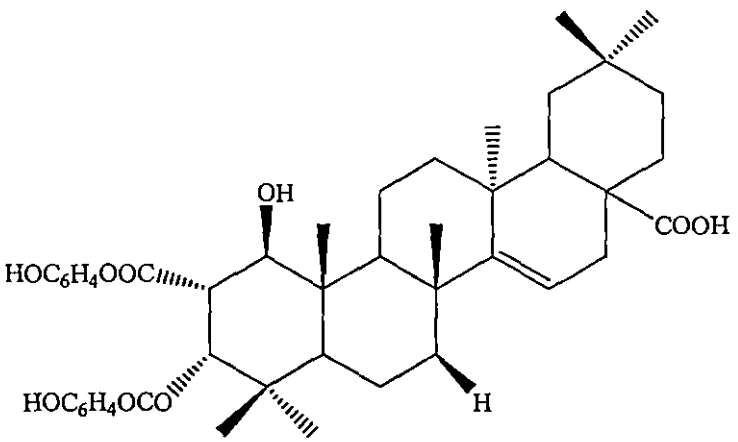
Antonia *et al.*[4] extracted lupane triterpenoid lupeol, the ursane triterpenoid α–amyrin and esters of these compounds from the bark of roots of *Alstonia boonei* and observed that those compounds had anti-inflammatory properties. They found that α–amyrin was a competitive inhibitor of bovine trypsin and chymotrypsin; lupeol linoleate, lupeol palmitate and α–amyrin linoleate were non-competitive inhibitor of chymotrypsin. They also found that lupeol, α–amyrin, palmitic and linoleic acid esters of these compounds were very weak inhibitors of porcine pancreatic elastase and of *Lucilia cuprina* and *Helicoverpa punctigera* leucine aminopeptidases.

Li *et al.*[5] extracted a new lupane type triterpenoid, 3β, 11α–dihydroxy-30-norlupan-20-one and six known lupane triterpenoids from the whole plant of *Salvia roborowskii maxim* using petroleum ether as a solvent. They elucidated their structures by means of spectral methods including NMR and MS techniques.

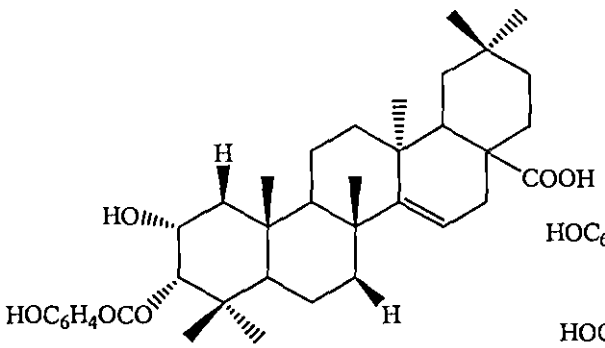
Tostikoya *et al.*[6] studied the biological activity of natural and semi synthetic lupane triterpenoid and discussed in two-part review. The first part was devoted to the pharmacological properties of natural lupane triterpenoids. They reported that betulinic acid proved to be the most effective antitumor agent among more than fifty natural lupines.

Kanokmedhakul *et al.*[7] isolated a new 1,3-dihydroxy-2-methyl-5,6-dimethoxyanthraquinone [a], six known anthraquinones [b], nordamnacanthal [c], damnacanthal ,rubiadin [d], rubiadin-1-methylether [e], lucidin-ω-methylether [f] and 1-hydroxy-2-hydroxymethyl-3-methoxyanthraquinone [g], a β-sitosterol, together with two known triterpenoids, β-acetylolean-12-en-28-olicacid [h] and 3β-O-acetyl-11α,12α-epoxyolean-28,13-olide [i] from the roots and stems of *Prismatomeris fragrans*. Their structures were established on the basis of spectral data. They studied the antiplasmodial, antituberculosis, antifungal and anticancer cell lines tests of the isolated compounds and the bioactivity assays showed that only **i** exhibited moderate antimalarial activity, **b** and **c** exhibited antifungal activity while **b, c, d, g** and **i** showed antituberculosis activity. In addition, compounds **b, c** and **g** exhibited cytotoxicity to BC cell line while **a,** (the methyl ether derivative of **1**), **b, c, d, e,** and **i** exhibited cytotoxicity to NCI-H187 cell line.

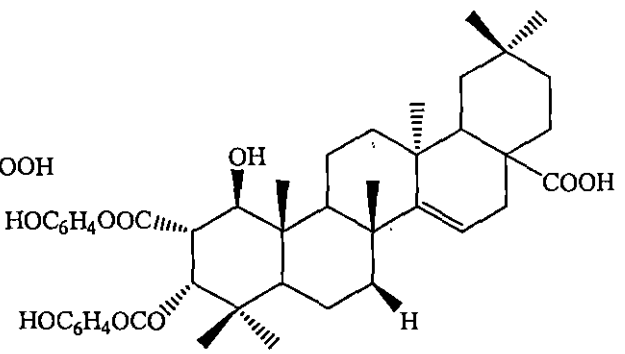
Chaudhuri *et al.*[8] isolated pentacyclic triterpenoids based on the taraxer-14-ene skeleton with a C-28 attached carboxylic acid group from the roots of *Maprounea africana*. They identified these compounds as 1β, 2α-dihydroxyaleuritolic acid 2,3-bis-hydroxybenzoate,2α-hydroxyaleuritolic acid 3-*p*-hydroxybenzoate, 2α-hydroxyaleuritolic acid 2,3-bis-*p*-hydroxybenzoate, aleuritolic acid 3-*p*-hydroxybenzoate, aleuritolic acid, and aleuritolic acid 3-acetate. They reported that compounds 1β, 2α-dihydroxyaleuritolic acid 2,3-bis-hydroxybenzoate, were new triterpene esters.



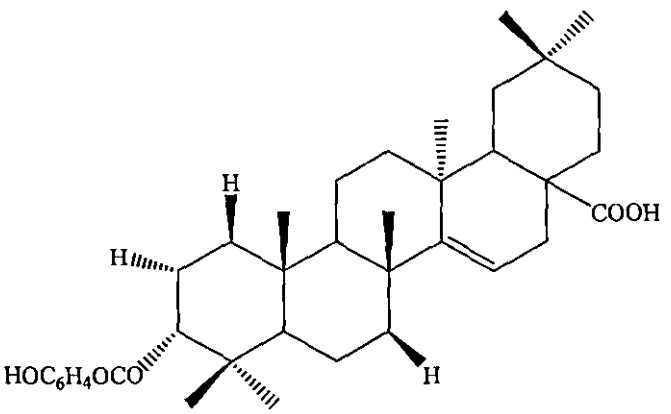
1β, 2α-dihydroxyaleuritolic acid 2,3-bis-hydroxybenzoate (11)



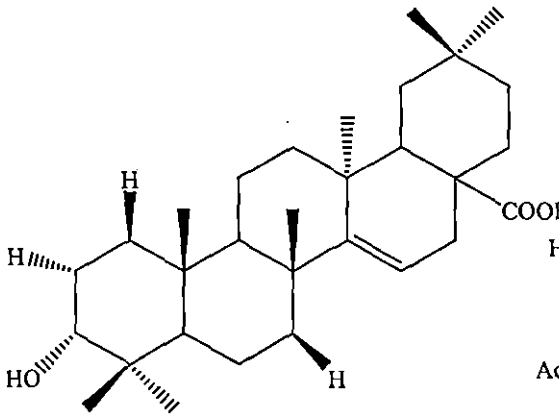
2α-hydroxyaleuritolic acid 3-p-hydroxybenzoate (12)



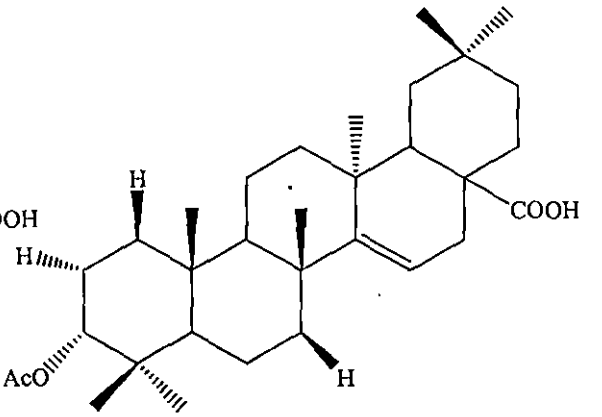
2α-hydroxyaleuritolic acid 2,3-bis-p-hydroxy benzoate(13)



Aleuritolic acid-3-p-hydroxybenzoate (14)

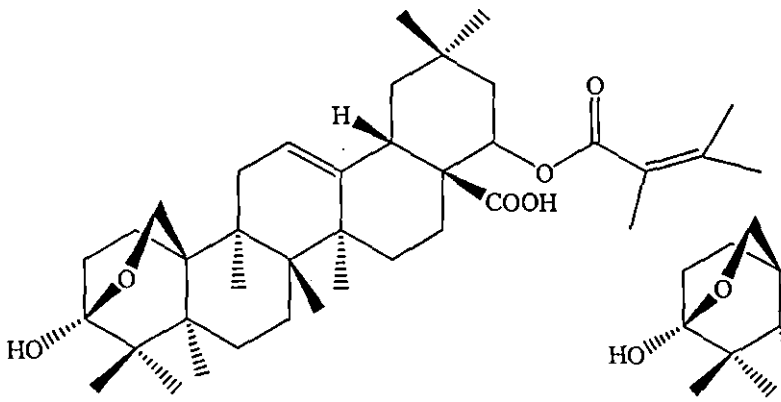


Aleuritolic acid (15)

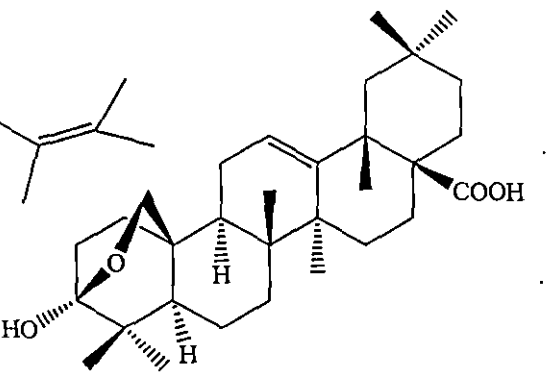


Aleuritolic acid 3-acetate (16)

Begum *et al.*[9] isolated three new pentacyclic triterpenoids, camaryoloic acid, methylcamaralate and camangeloyl acid with six known compounds, β-sitosterol 3-O-β-D-glucopyranoside, octadecanoic acid, docosanic acid, palmitic acid, camaric acid and lantanolic acid from the aerial parts of *Lantana camara*. They elucidated the structures of the new compounds by spectroscopic and chemical methods.



Camaric acid (17)



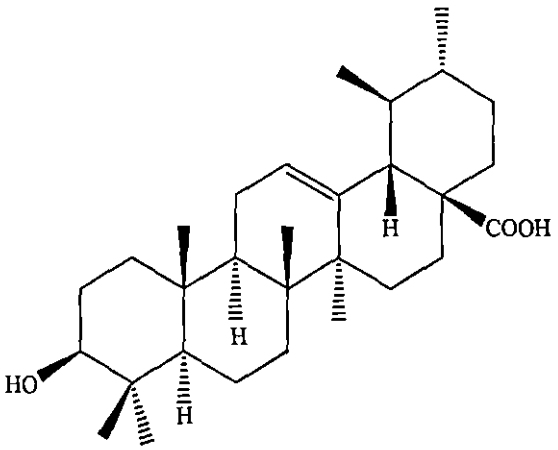
lantanolic acod (18)

Rahaman *et al.*[10] reported that two new triterpenoids, 18α,19 β-20(30)taraxasten-3β,21α-diol (cichoridol) and 17-epi-methyl-6-hydroxyangolensate (intybusoloid) obtained from the methanolic extract of seeds of *Cichorium intybus* (Asteracae) along with eleven known compounds, lupeol, friedelin, betunaldehyde, syrginic acid, vanillic acid, 6,7-dihydroxycoumarin and methyl-alpha-D-galactopyranoside Compound.

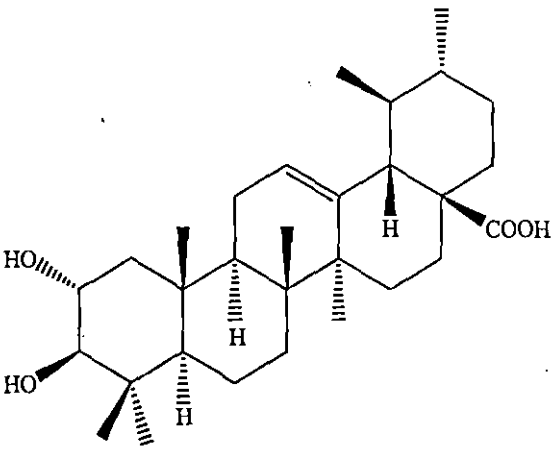
Choudhury *et al.*[11] reported the biotransformation of a pentacyclic triterpene, oleanolic acid, with *Fusarium lini* afforded two oxidative metabolites, 2α,3β–dihydroxy-olean-12-en-28-oic acid, and 2α, 3β, 11β–trihydroxyolean-12-en-28-oic acid. They also found that metabolite 3 was a new compound. The structures were characterized on the basis of spectroscopic studies. These metabolites exhibited a potent inhibition of α–glucosidase enzyme and thus were effective in diabetes by delaying the glucose absorption.

Begum *et al.*[12] isolated two triterpenoids, 20β-acetoxy-2a,3β-dihydroxyrus-12-en-28-oic acid (guavanoic acid, 3) and 2α,3β-dihydroxy-24-*p*-z-coumaroyloxyrus-12-en-28-oic acid (guavacoumaric acid, along with six known compounds such as 2α-hydroxyursolic acid, jacoumaric acid, isoneriucoumaric acid, asiatic acid, ilelatifol D and β-sitosterol-3-O-β-D-glucopyranoside from the leaves of *Psidium guajava*. They determined the structures of the isolated compounds through spectroscopic methods.

Shai *et al.*[13] isolated four compounds (lupeol, betulinic acid, ursolic acid and 2 alpha-hydroxyursolic acid) from the leaves of *Curtisia dentata*. They studied the antibacterial and antifungal activity (using broth microdilution assay and bioautography method) and found that betulinic acid, ursolic acid and 2α-hydroxyursolic acid appreciably inhibited fungal growth with MIC values ranged between 8 to 63 μg/mL.



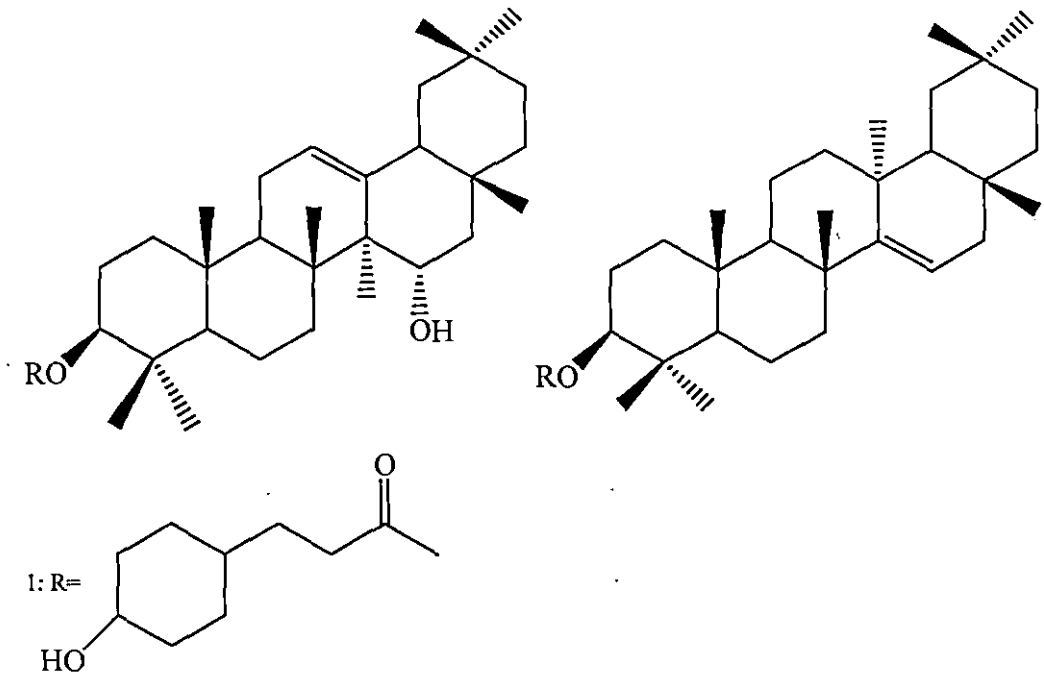
Ursolic acid (19)



2-α-hydroxyursolic acid (20)

Gu *et al.*[14] derived three pentacyclic triterpenoids from *Valeriana laxiflora* DC ,*Lavandula dentate* L.,*Tanacetum parthenium* (L.) Sch. Bip.as oleanolic acid, betulinic acid and ursolic acid and found that the isolated triterpenoids were moderate anti-tubercular in a microplate alamar blue assay.

Li *et al.*[15] isolated seven pentacyclic triterpenoids including 3β–O–coumaryl-β–amyrin [fig.21], 15α–hydroxy, β–amyrin [fig.22], 3β–taraxerol [fig.23], 3β–taraxerol formate [fig.24], 3β–taraxerolacetate [fig.25], 3β–O–(E)–coumaryl-taraxerol [fig.26] and 3-β-*o*-(Z)-coumaroyl-taraxerol [fig.27] from the stems and twigs of the mangrove plant *Rhizophora stylosa* (Rhizophoraceae). The structures of the isolated compounds were determined by extensive analysis of their spectroscopic data. Among the metabolites, compound **1** was a new olenane type terpenoid coumaroyl ester, while compound **4** was a new natural product.



21: R = 3β–O–coumaryl

22. R=H=15α–hydroxy, β–amyrin

23. R=H=3β–taraxerol

24. R=Formyl=3β–taraxerol formate

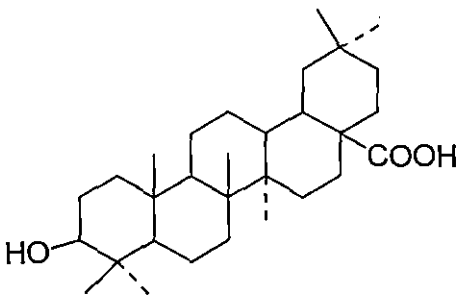
25. R=Acetyl=3β–taraxerol acetate

26. R=E-coumaryl=3β–*o*–(E)–coumaryl-taraxerol

27. R=Z-coumaryl=3–β-*o*- (Z)-coumaroyl-taraxerol

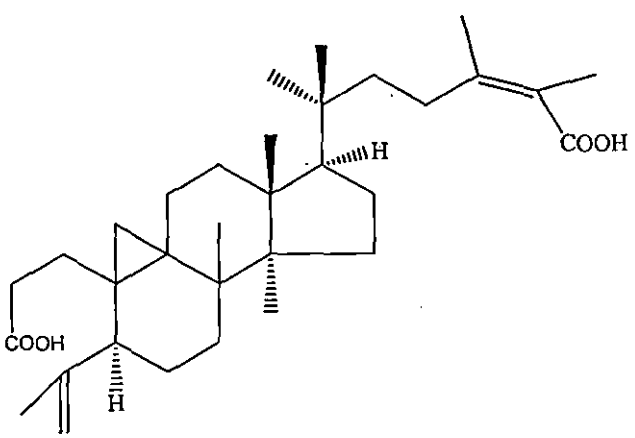
Pichai *et al.*[163] extracted the powdered material of "Vidattali" equated to *Dichrostachys cinerea* and separated n-octacosanol, β–sitosterol, friedelin, epifridelinol, α-amyrin and β–sitosterol-3-β-D-glucopyranoside from the aerial part. They studied antibacterial and antifungal activities of n-hexane and chloroform extracts on three bacteria (*Escherichia coli*, *Pseudomonas aeruginasa* and *Staphylococcus aureus*) and two fungi (*Aspergillus flavus* and *Mucor* sp.) at 1.25, 2.5, 5.0 and 10 mg/mL concentrations. Study was made in nutrient agar and SDA mediums by steak method. They observed that the chloroform extract showed moderate antibacterial efficacy towards *E.coli* and

Staphylococcus at higher concentrations (5-10 mg/mL). Antifungal activities of the extracts against *Aspergillus* and *Mucor* were also observed at higher concentrations.

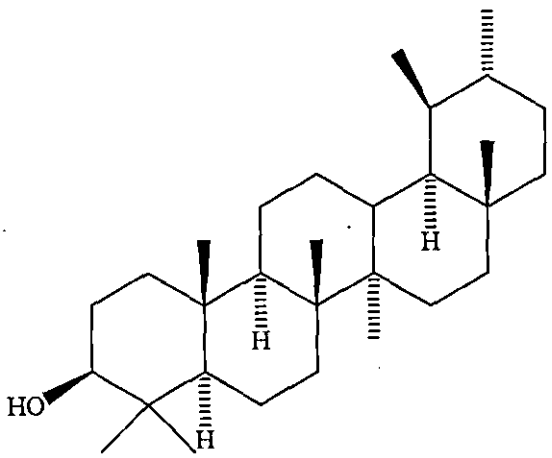


Oleanolic acid (28)

Sun *et al.*[17] isolated a ring-secocycloartene triterpenoid, nigranoic acid (3,4-secocycloarta-4(28),24-(Z)-diene-3,26-dioic acid from the stem of *Schisandra sphaerandra*, a Chinese traditional medicinal plant. The structure elucidation and unambiguous NMR spectral assignment were achieved by the combination of 1D and 2D-NMR techniques with the aid of computer modeling. They found that nigranoic acid showed activity in several anti-HIV reverse transcriptase and polymerase assays.



Nigranoic acid (3,4-secocycloarta-4(28),24-(Z)-diene-3,26-dioic acid (29)



α-amyrin (30)

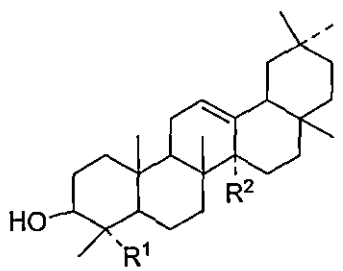
Chi::ozem *et al.*[18] isolated two new friedelane-type triterpenes named 12-alpha-hydroxyfridelane-3,15-dione and 3-beta-hydroxyfriedelan-25-al, together with six known compounds from the stems of *Drypetes paxii* Hutch (Euphorbiaceae) and established their structures. They also tested the antimicrobial activity of the five friedelane-type triterpenes, one olean-12-ene triterpene saponin against some Gram-positive and Gram-negative bacteria and they appeared to be modestly active.

Angeh *et al.*[19] isolated four known triterpenoids, 11-alpha,3-beta-dihydroxy-12-oleanen-29-oic acid, 1-hydroxy-12-olean-30-oic acid, 3,30-dihydroxyl-12-oleanen-22-one and 1,3,24-trihydroxyl-12-olean-29-oic acid along with a new pentacyclic triterpenoid (1-alpha, 23-dihydroxy-12-oleanen-29-oicacid-3beta-O-2, 4-di-acetyl-L rhamnopyranoside) through a bioassay-guided procedure from the leaves of *Combretum imberbe*. The structures of the compounds were elucidated on the basis of 1D and 2D NMR experiments, as well as mass spectrometric data. They observed that all the isolated compounds have moderate (62 μg/mL) to strong (16 μg/mL) antibacterial activity (MIC values) against *Staphylococcus aureus* and *Escherichia coli*, with 1 and 5 being most active. The results of the study gave credence to the ethnomedicinal use of *Combretum imberbe*.

Mathabe *et al.*[20] extracted four known compounds, two triterpenoids, compound 1 [d-friedoolean-14-en-oic acid (3-acetyl aleuritolic acid)] and compound 2 (lupeol), and two diterpenes, compound 3 [2,6alpha-dihydroxy-norbeyer-1,4,15-trien-3-

one (diosphenol 2)] and compound 4 (3beta-hydroxy-beyer-15-ene-2-one) from the bark of *Spirostachys africana* using ethanol as a solvent . They tested the antibacterial activity of the isolated compounds using micro-dilution method Compound 1, exhibited minimum inhibitory concentration (MIC) of 50μg/mL against *Staphylococcus aureus, Salmonella typhi, Vibrio cholera, Escherichia coli* and *Shigella dysentery.*

Wada *et al.*[21] isolated lupane and oleanane type triterpenoids from the bark of *Phyllanthus flexusus* and screened inhibitory activity on human Topos (topoisomerases) I and II. They found that olean-12-en-3β, 15α-diol, olean-12-en-3β, 15α, 24-triol, lupeol, and betulin were selective catalytic inhibitors of human Topo II activity with IC_{50} values in the range of 10-39 μM/mL.

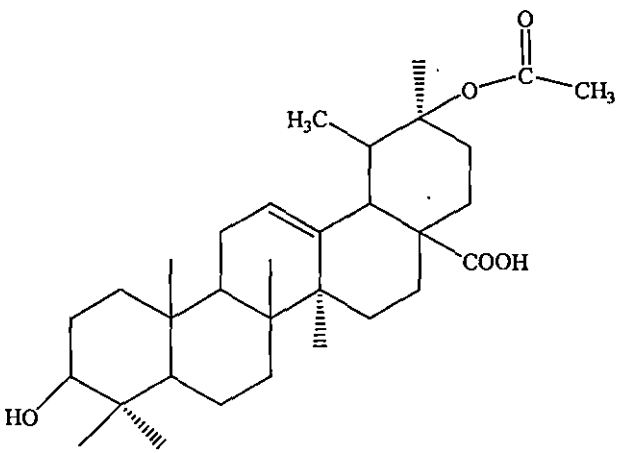


	R^1	R^2	
31	Me	OH	= olean-12-en-3,15-diol
32	CH_2OH	OH	= olean-12-en-3, 15, 24-triol

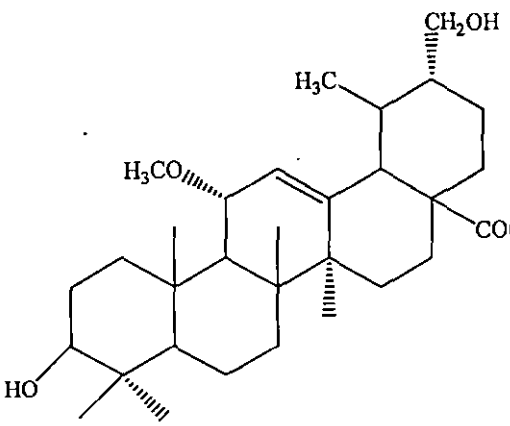
Siddiqui *et al.*[22] investigated the constituents of the fresh, uncrushed leaves of *Eucalyptus camaldulensis* var. *obtusa* and isolated a triterpenoid (amirinic acid) with four known triterpenoids ursolic acid lactone, betulinic acid, oleanolic acid and ursolic acid. They transformed amirinic acid into amirolide in deuterated chloroform at room temperature. The new products were characterized by exhaustive spectroscopic studies.

Siddiqui *et al.*[23] studied the fresh leaves of *Carissa carandas* collected from the Karachi Region in Pakistan and isolated four pentacyclic triterpenoids including one new constituent carissin and two hither to unreported compounds. They elucidated the structure of the new compound as 3beta-hydroxy-27-E-feruloyloxyurs-12-en-28-oic acid.

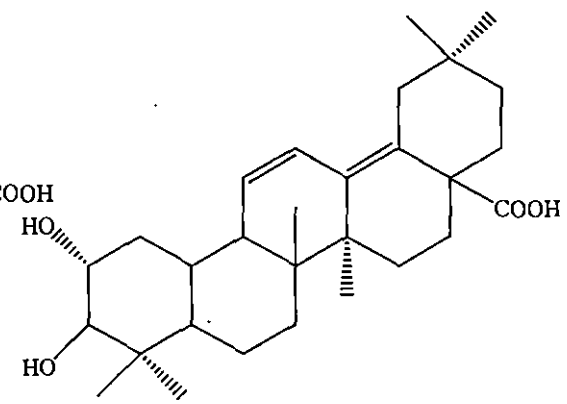
Begum and Siddiqui[24] investigated the constituents of fresh, uncrushed leaves of *E. camaldulensis* var. *obtuse* and isolated a known and 3 new triterpenoids. They characterized the new compounds by chemical and spectroscopic studies as camaldulic acid (20 beta-acetoxy-3 beta-hydroxyrus-12-en-28-oic acid), camaldulensic acid (3-beta, 30-dihydroxy-11 alpha-methoxyrus-12 en-28-oic acid) and camaldulenic acid (2-alpha, 3-beta-dihydroxyolean-11,13(18)-dien-28-oic acid)



Camaldulic acid (33)



Camaldulensic acid (34)



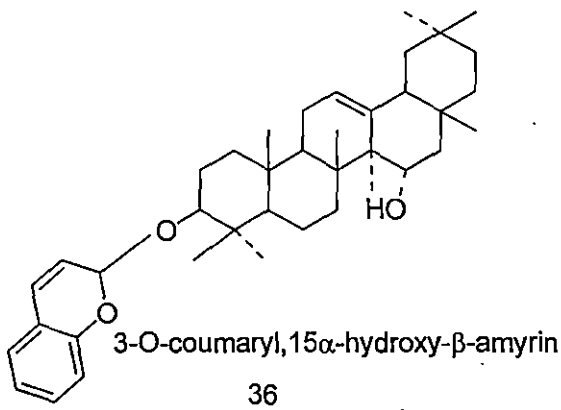
Camaldulenic acid (35)

Setzer *et al.*[25] extracted the crude from the bark of *Syncarpia glomulifera* using chloroform as a solvent and reported antibacterial and cytotoxic activity. They isolated

oleanolic acid-3-acetate, ursolic acid-3-acetate and betulinic acid from the bark. They observed that the relatively large abundance (10 % of the crude extract) and high degree of activity of betulinic acid were responsible for the bioactivity of the crude bark extract.

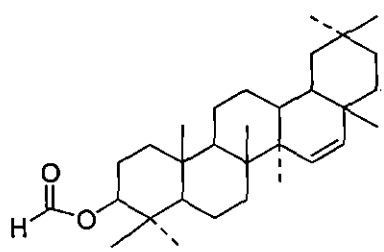
Lutskii *et al.*[26] isolated triterpenoids from the plants of the *Thalictrum sp* and the structural, chemical and spectral properties were systematized for the first time. They discussed the features of the ^{13}C NMR spectra of cycloartane triterpenoids.

Li *et al.*[27] isolated seven pentacyclic triterpenoids including 3β-*O*-(*E*)-coumaroyl-15α-hydroxy-β-amyrin [fig.36], 15α–hydroxy-β-amyrin, 3β-taraxerol, 3β-taraxerol formate [fig.37], 3β-taraxerol acetate [fig.38], 3β-*O*-(E)-coumaroyl-taraxerol [fig.39], and 3β-*O*-(*Z*)-coumaroyl-taraxerol from the stems and twigs of the mangrove plant *Rhizophora stylosa*. The structures of the isolated compounds were determined by extensive analysis of their spectroscopic data. They reported that among these metabolites, compound fig.36 was a new oleanane-type triterpenoid coumaroyl ester, while compound fig.37 was a new natural product obtained here as an isolated substance for the first time.

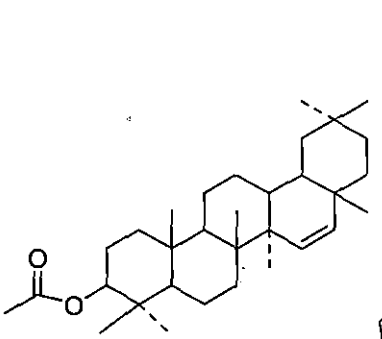


3-O-coumaryl,15α-hydroxy-β-amyrin

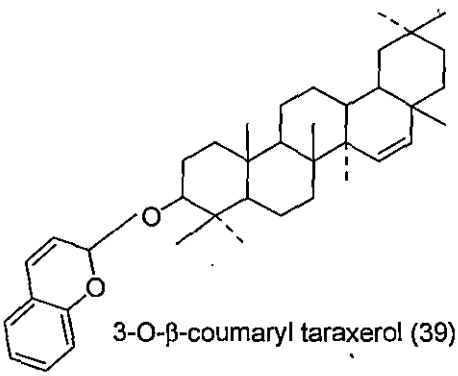
36



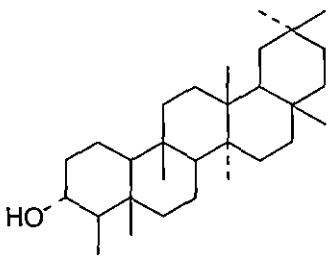
3β-taraxerol formate (37)



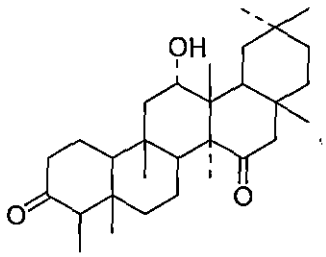
3β-taraxerol acetate (38)



3-O-β-coumaryl taraxerol (39)



3-epifridelinol (40)



12α–hydroxy-3,15-friedelin dione (41)

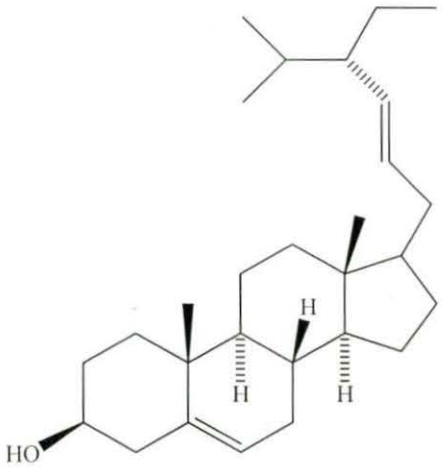
Xu *et al.*[28], isolated Geumonoid, a new triterpene from *Geum japonicum* and its structure was elucidated on the basis of 1D, 2D NMR and MS spectroscopic analysis. They observed that Geumonoid showed inhibitory activity against HIV-1 protease.

He *et al.*[29]. isolated the chemical constituents of the roots of *Aconitum taipeicum* (Ranunculaceae) and purified using silica gel column chromatography. They found new norditerpenoid alkaloids, isodelelatine along with five known alkaloids. The structure of the new compound was elucidated on the basis of spectral data.

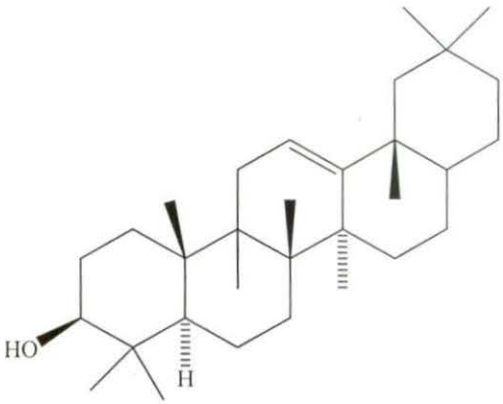
Srikrishna *et al.*[30] carried out antibacterial activity using cup plate method by petroleum ether, chloroform, methanol and water extract of the bark of *Aporosa lindleyana* (Euphorbiaceae). They observed that the compounds showed moderate to very good activity against *Bacillus subtilis, Escherichia coli* and the data were compared with the standard drug tetracycline. They studied the antifungal activity against *Penicillium chrysogenous, Candida albicans, Aspergilus niger* and *Trichoderma viridi* and compared with the standard drug fluconazole. The petroleum ether extract showed considerable

activity towards all the four fungal organisms. Analgesic activity has been carried out on Swiss albino male mice by abdominal constriction method. All the extracts showed

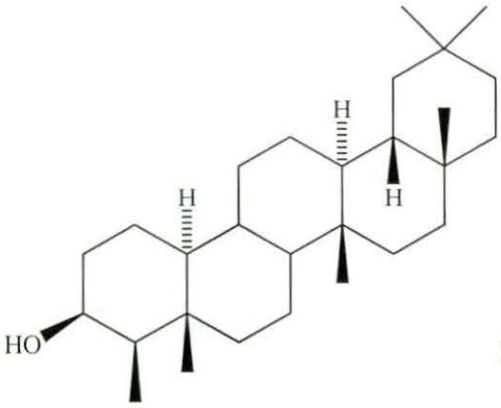
Singh *et al.*[31] extracted a mixture of steroids and triterpenoids: β–sitosterol, stigmasterol, β–amyrin, friedelan-3β–ol (epifridelenol), cycloartenone, β–amyrin acetate, friedelin and epi-friedenyl acetate from *Heliotropium marifolium* using hexane as a solvent. They tested the isolated triterpenoids against selected pathogenic bacteria and fungi, e.g. *Escherichia coli, Staphylococcus aureus, Aspergillus niger and Penicillium chrysogenum.* They also discussed the quantification and assessment of their growth inhibitory potency and found that cycloartenone was the major triterpenoids in both *in vivo* and *in vitro* cell culture.



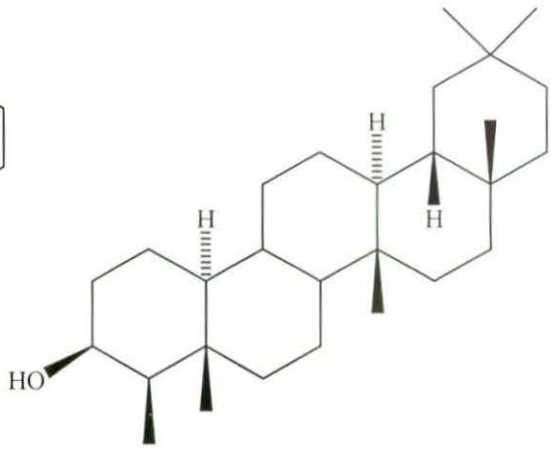
Stigmasterol (42)



Betaamyrin (43)



Friedelan-3β-ol (44)



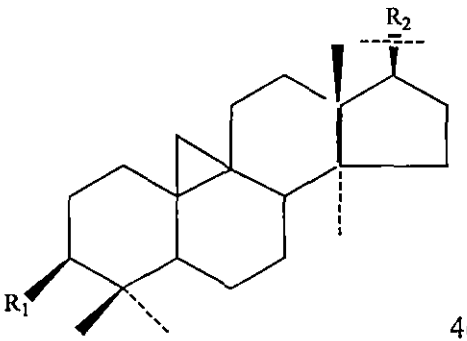
3β-hydroxy friedilane (45)

Sukul and Chaudhuri[32], extracted the leaves of *Lantana camara* using different solvents. They observed that four fractions of petroleum ether extract showing significant antibacterial activity against some human pathogens under *in vitro* conditions. The MIC of the methanol fraction, containing triterpenoids, active against these pathogens was found to be comparable with those of some therapeutically used antibiotics.

Panizzi *et al.*[33] isolated some constituents from the flowering aerial parts of *Geum rivale* and studied their antimicrobial activity on bacteria and fungi. The activity was more in the triterpene fractions for Gram-positive and Gram-negative bacteria; activity was also toward flavonoid fractions.

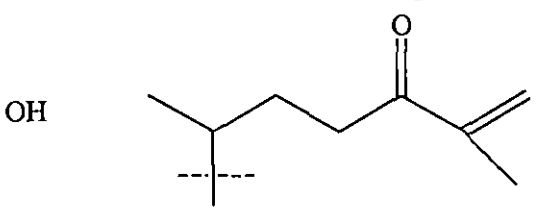
Takeoka *et al.*[34] isolated three triterpenoids betulinic acid, oleanolic acid and ursolic acid as their methyl esters from diethyl ether extracts of almond hulls using flash chromatography and preparative high performance liquid chromatography. They were characterized triterpenoids using chromatographic and spectroscopic methods and these studies demonstrated that almonds hulls were a rich source of triterpenoids. They reported anti-inflammatory, anti-HIV and anti-cancer activities of these triterpenoids.

Madureira *et al.*[35] carried out phytochemical re-investigation of the whole plant of *Euphorbia segetalis* and isolated five tetracyclic triterpenes: 3β-hydroxy-cycloart-25-en-24-one, cycloart-25-ene-3β,24-diol, cycloart-23-ene-3β,25-diol, lanosta-7,9(11),24-trien-3β-ol and lanosta-7,9(11),24(31)-trien-3β-ol, 3β-acetoxy-cycloart-25-en-24-one and glutinol, lupenone, friedelin dammaranodienol, cycloartenol acetate, 24-methylenecycloartanol acetate and β-sitosterol. They were studied for their antiviral activities against Herpes simplex virus (HSV) and African swine fever virus (ASFV) and observed that lupenone exhibited strong viral plaque inhibitory effect against HSV-1 and HSV-2. The *in vitro* antifungal and antibacterial activities of cycloart-23-ene-3β,25-diol, was also investigated.



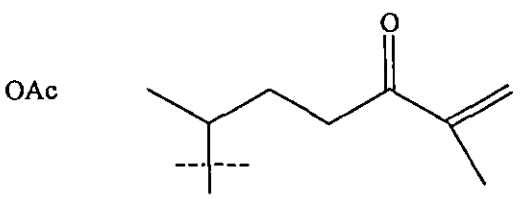
46-51

R1 R2

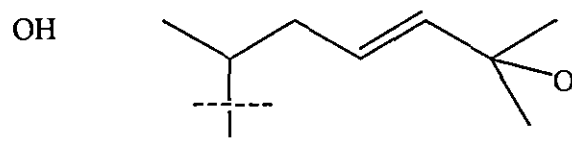


= 3 β-hydroxy-cycloart-25-en-24-one

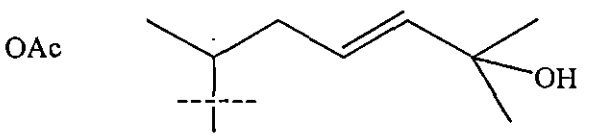
R1 R2



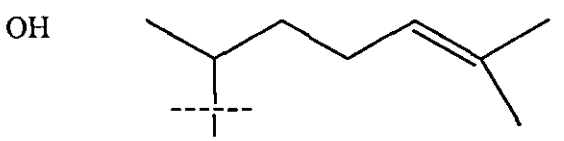
= 3β-acetoxy-cycloart-25-en-24-one



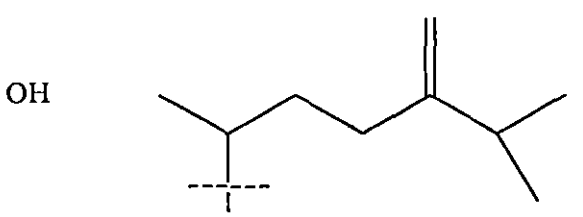
= cycloart-25-ene-3β,24-diol



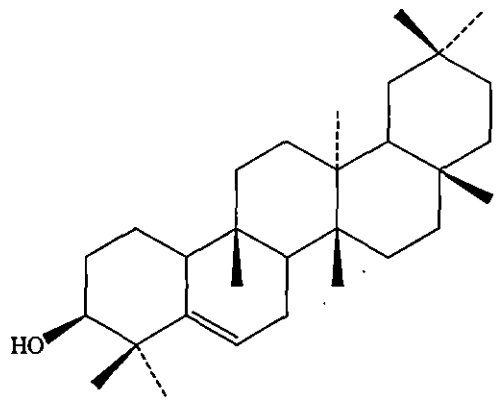
= cycloart-23-ene-3β,25-diol



= cycloartenol

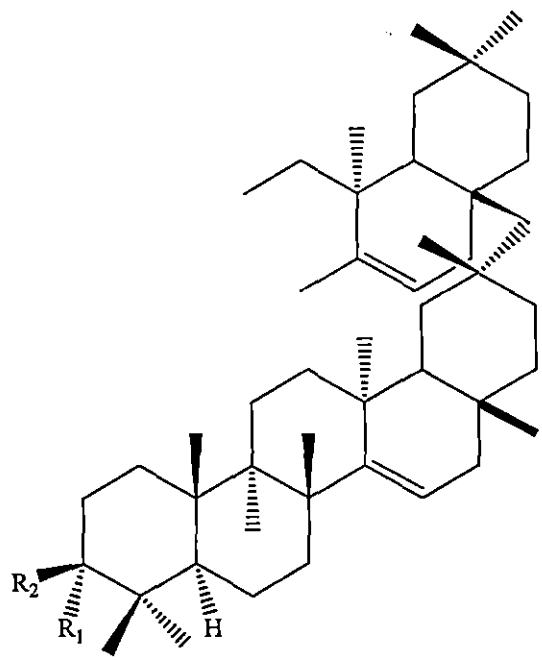


= 24-methylenecycloartanol



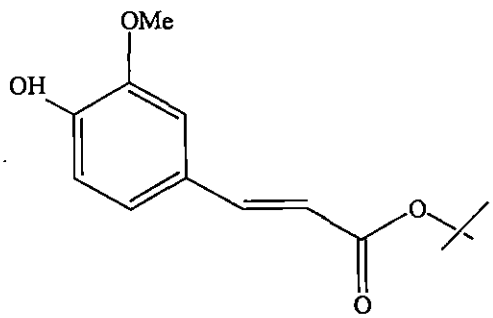
Glutinol (52)

Laphookhieo *et al.*[36] isolated six new pentacyclic triterpenoids esters (fig.53-58) together with 3α- and 3β-tarexerol from the fruits of *Bruguiera cylindrica*. The structures of the new compounds were characterized as 3α-E-feruloyltaraxerol (fig.53), 3α-Z-feruloyltaraxerol (fig.54), 3 β-E-feruloyltaraxerol (fig.55), 3 β–Z-feruloyltaraxerol (fig.56), 3α-E-coumaroyltararaxerol (fig.57), and 3α-Z-coumaroyltaraxerol (fig.58). They reported that compounds 2 and 6 exhibited weak cytotoxicity against the NCl-H187 cell line.



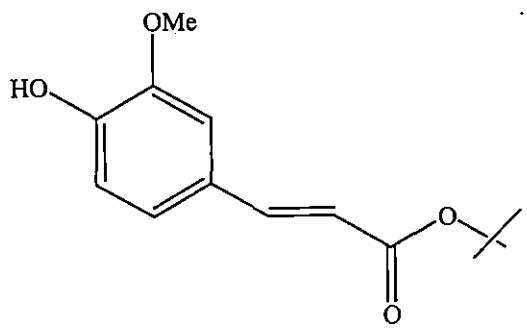
53

R_1 R_2

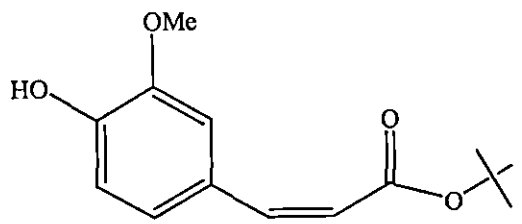


H = 3α–E-feruloyltaraxerol

54

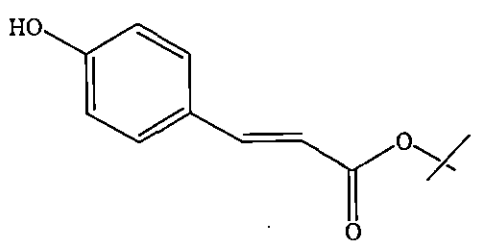


H = 3β–E-feruloyltaraxerol

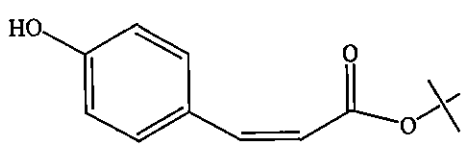


H =3β–Z-feruloyltaraxerol

55,56



H = 3α–E–coumaroyltaraxerol

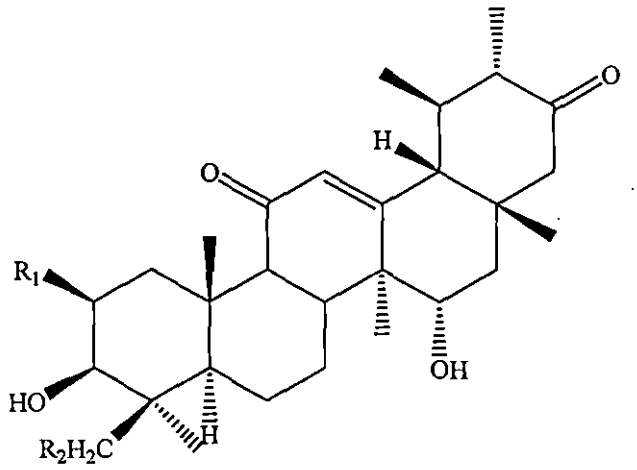


H =3β–Z–coumaroyltaraxerol

57,58

Araujo and Chaves [37] isolated eleven oleanane, ursane and lupane-type triterpenes daturadiol (3β,6β–dihydroxy-olean-12-ene), 3β-hydroxy-30-norlupan-20-one, lupenone, β-amyrenone, α–amyrenone, lupeol, β-amyrin, α–amyrin, betulin, erythrodiol and uvaol, in addition to squalene, sitosterol and α–tocopherol from the leaves of *Terminalia brasiliensis* Camb. They identified the structures of these compounds by ^{1}H and ^{13}C NMR spectral analysis.

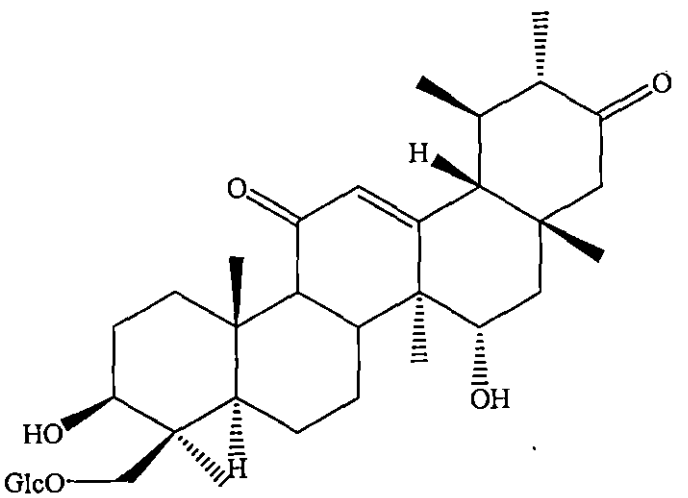
Ghosh *et al.*[38] extracted seeds of *Swietenia mahagoni* using methanol as a solvent and reported pharmacological activity including anti-inflammatory activity of the extract. They evaluated the anti-inflammatory activity using acute, sub-chronic, and chronic models of inflammation in rodents. The antipyretic and analgesic activities were evaluated in mice models. They studied the acute toxicity of the extract using different doses and the effect was compared with the standard drug, ibuprofen. The results revealed that the extract produces anti-inflammatory activity through dual inhibition. Zhou *et al.*[39] isolated three new triterpenoids: 11,21-dioxo-2beta,3beta, 15alpha-trihydroxyurs-12-ene-2-O-beta-D-glucopyranoside,11,21-dioxo-3-beta,15-alpha, 24-trihydroxyurs-12-ene-24-O-beta-D-glucopyranoside, and 11,21-dioxo 3-beta,15-alpha,24-trihydroxyolean-12-ene-24-O-beta-D-glucopyranoside, and two new flavonoids viz.apigenin-7-O-[2"-O-(5"'-O-feruloyl)-beta-D-apiofuranosyl]-beta-glucopyranoside and chrysoeriol-7-O-[2"-O-(5"'-O-feruloyl)-beta-D-apiofuranosyl]-beta-d-glucopyranoside from the whole plant of fresh *Apium graveolens* together with 10 known flavonoids. The structures of the new compounds were elucidated by analysis of spectroscopic data. They evaluated the inhibitory effects of the compounds isolated on nitric oxide production in lipopolysaccaride-activated macrophages.



1 R_1=OGlc, R_2=H ; 11,21-dioxo-2beta,3beta,15alpha-trihydroxyurs-12-ene-2-O-beta-D-glucopyranoside

2R_1=H R_2=OGlc ; 11,21-dioxo-3beta,15alpha,24-trihydroxyurs-12-ene-24-O-beta-D-glucopyranoside

59



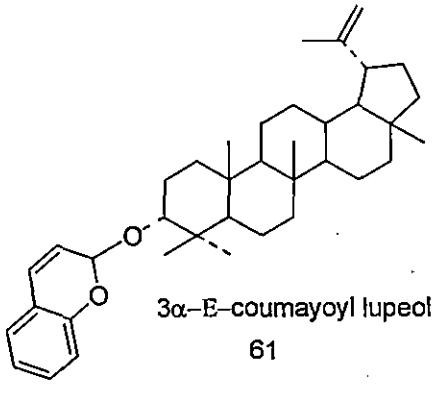
3 = 11,21-dioxo-3beta,15alpha,24-trihydroxyolean-12-ene-24-O-beta-D-glucopyranoside

(60)

Siddiqui *et al.*[40] isolated nine pentacyclic triterpenoids along with a coumarin from a fresh, undried and uncrushed spring leaves of *Plumeria obtuse*. They

characterized the new triterpenes obtusin and obtusilic acid as the 24-E and 27-Z-*p*-coumaric esters of the novel 3β,24-dihydroxyrus-12-en-28-oic acid and 3β,27-dihydroxyrus-12-en-30-oic acid respectively through chemical and spectral studies while the other eight compounds identified were known kaneroside, oleandrin, α-amyrin, neriucoumaric acid, isoneriucoumaric acid, alphitolic acid, oleanonic acid, methyl *p*-E-coumarate and scopoletin.

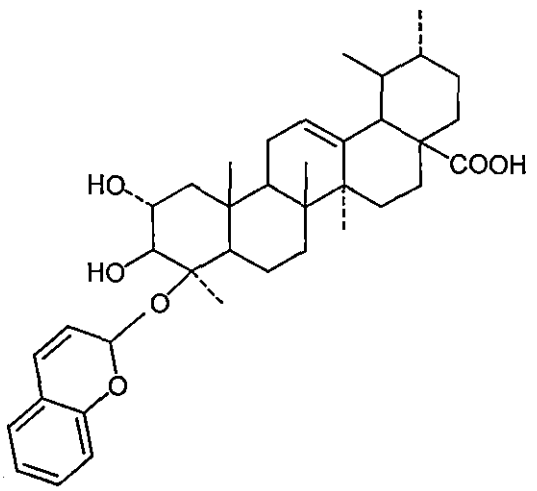
Karalai and Laphookhieo[41] isolated three new pentacyclic triterpenoid esters together with six known lupane-type triterpenoids from *Bruguiera cylindrica.* They elucidated the structures of the new compounds by spectroscopic methods and were characterized as 3α-E-coumaroyllupeol, 3α-Z-coumaroyllupeol and 3α-E-caffeoyltaraxerol.



3α–E–coumayoyl lupeol

61

Begum *et al.*[42] isolated three pentacyclic triterpenoids including one new and two known obtusinin and goreishic acid from the leaves of *Psidium guajava.* They characterized the new constituent as 2α-hydroxy-3β-*p*-E-coumaroyloxyurs-12, 18-dien-28-oic acid through 1 H-NMR and 13 C-NMR. They isolated compound guajavanoic acid first time from the genus *Psidium.*

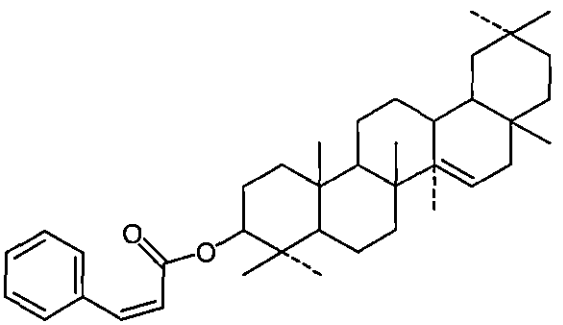


2α,3β-dihydroxy-24-p-E-coumaroyloxyurs-12-en-28-oic acid

62

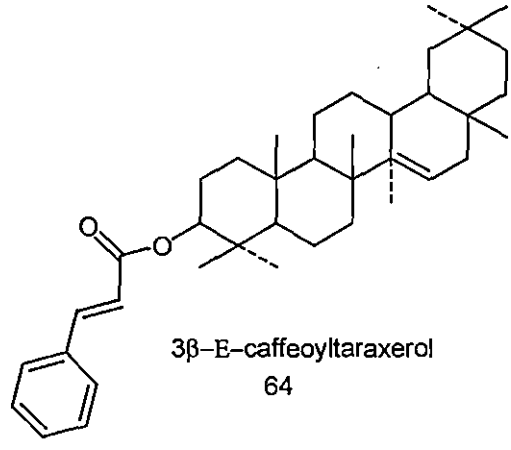
Larshini *et al.*[43] extracted 12 plants, selected on the basis of the folk-medicine reports and examined their anti bacterial effects against eight pathogenic bacteria. They found that the n-butanol extract of *Calotropis procera* flowers and the aqueous extract of *Eugenia caryophyllata* were the most effective against the bacteria they tested.

Laphookhieo *et al.*[44] isolated a new sesquiterpene and two new pentacyclic triterpenoid esters together with three known compounds from the fruits of *Rhizophora mucronta*. They elucidated the structures of the isolated compounds and characterized as 3-hydroxy-3,7,11-trimethyl-9-oxododeca-1,10-diene, 3β-E-caffeoyltaraxerol and 3β-Z-caffeoyltaraxerol.



3β–Z–caffeoyltaraxerol

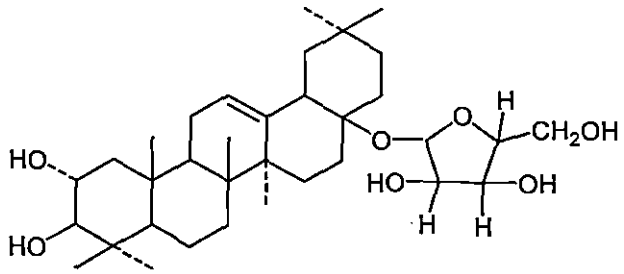
63



3β–E–caffeoyltaraxerol
64

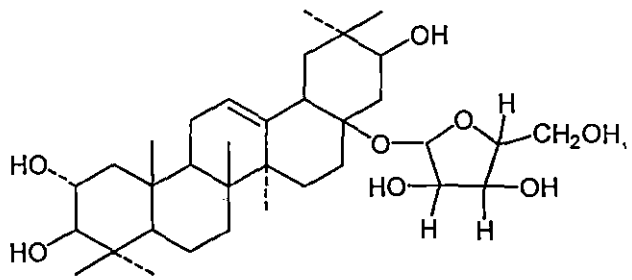
Ibrahim and Ali[45] isolated a long chain ketone, a pentacyclic triterpenoid coupled with fatty acid moiety, and an acyclic diterpenoid from the ethanol soluble part of *Nepeta crassifolia* collected from Kangavar, Iran. They elucidated the structures of all the metabolities with the aid of spectroscopic techniques, including 2D NMR experiments.

Tabopda *et al.*[46] isolated four new triterpene glucosides (**a-d**) using methanol as a solvent from the stem bark of *Terminalia superba*. The structures of the new compounds were established by spectroscopic method and characterized as 2-alpha,3-beta-dihydroxyolean-12-en-28-oic acid 28-O-beta-D-glucopyranoside (**a**), 2-alpha,3-beta,21 beta-trihydroxyolean-12-en-28-oic acid 28-O-beta-D-glucopyranoside (**b**), 2-alpha,3-beta,29-trihydroxyolean-12-en-28-oic acid 28-O-beta-D-glucopyranoside (**c**) and 2-alpha,3 -beta,23,27-tetrahydroxyolean-12-en-28-oic acid 28-O-beta-D-glucopyranoside (**d**) together with the known triterpene 2-alpha,3-beta,23-trihydroxyolean-12-en-28-oic acid (**e**). They investigated the antibacterial activity of **a-e** against two gram-positive bacteria (*Bacillus subtilis, Staphylococcus aureus*), and four Gram-negative (*Escherichia coli, Shigella flexenari, Pseudomonas aeruginosa, Salmonella typhi*) bacterial strains.



2α,3β-dihydroxyolean-12-en-28-oic acid-28-pyranoside

65



2α,3β,21β-trihydroxyolean-12-en-28-oic acid-28-pyranoside

66

2. Potential antimicrobial activities of triterpenoids and their derivatives

The reports presented by the earlier workers regarding the antimicrobial activity of various plant extracts were tested against different organisms. The observation (selective in manner) of the previous workers in concord with the present line of investigation have been presented in the following paragraphs.

Kumar *et al.*[47] carried out antimicrobial properties of a series of 61 medicinal plants belonging to 33 different families used in various infectious disorders at 1000 and 500 microg/ml concentration by agar dilution method against *Bacillus cereus, Bacillus pumilus, Bacillus subtilis, Bordetella bronchiseptica, Micrococcus luteus, Staphylococcus aureus, Staphylococcus epidermidis, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa , Streptococcus faecali, Candida albicans, Aspergillus niger and Saccharomyces cerevisiae.* They found that 28 plant extracts showed activity against at least one of the test organisms used. The crude extracts of *Jatropha gossypifolia, Aristolochia indica, Lantana camara, Cassia fistula* containing triterpenoid as chemical constituent exhibited significant antimicrobial activity and

property that support the folkloric use in the treatment of as broad-spectrum antimicrobial agents.

Adamu *et al.*[48] carried out a survey of medicinal plants used locally in the treatment of various diseases in Bauchi State-Nigeria and total 84 medicinal plants were listed chiefly containing triterpenoids. They investigated the antimicrobial activity of the aqueous extracts of the plants and found that out of 84 plants, 75 exhibited antimicrobial activity against one or more of the test organisms at a concentration of 200 mg/ml. They found that the extracts showed potentially interesting activity against *Proteus mirabilis, Pseudomonas aeruginosa, Staphylococcus aureus* and *Escherichia coli.*

Angeh *et al.*[49] isolated four known triterpenoids, 1alpha,3beta-dihydroxy-12-oleanen-29-oic acid (a), 1-hydroxy-2-olean-30-oic acid (b), 3,30-dihydroxyl-12-oleanen-22-one (c), and 1,3,24-trihydroxyl-12-olean-29-oic acid (d) along with a new pentacyclic triterpenoids (1alpha,23-dihydroxy-12-oleanen-29-oic acid-3beta-O-2,4-di-acetyl-L-rhamnopyranoside)(e) through a bioassay-guided procedure from the leaves of *Combretum imberbe*. They found that all the isolated compounds had moderate (62 µg/ml) to strong (16 µg/ml) antimicrobial activity (MIC values) against *Staphylococcus aureus, Escherichia coli,* and compound a and e was most active. The results of their study gave credence to the ethnomedicinal use of *Combretum imberbe* and biological activity of the metabolites.

Mothana *et al.*[50] studied the antiproliferative activity against three human cancer cells, antimicrobial activity against antibiotic susceptible three Gram-positive, three Gram-negative bacterial and one fungal stains and three multiresistant Staphylococcus strains by the agar diffusion method and the determination of MIC against three Gram-positive bacteria with the broth micro-dilution assay, as well as for their antioxidant activity using the DPPH radical scavenging method of sixty four methanolic and aqueous extracts of thirty Yemeni plants used in traditional medicine. They found that 12 plants showed growth inhibitory effect against all cancer cells with IC50 values< 50 µg/ml, 9 plants showed pronounced antimicrobial activity against Gram-positive bacteria among them multiresistant bacteria with inhibition zones>15 mm and MIC values < 500 µg./ml.

Shai *et al.*[51] isolated four compounds lupeol, betulinic acid, ursolic acid and 2-alpha-hydroxyursolic acid from the leaves of *Curtisia dentata*. They studied the antibacterial and antifungal activity using broth microdilution assay and bioautography method and found that betulinic acid and ursolic acid were antimicrobial.

Mansouri[52] found new antibacterial agents from ethanolic extracts of ten plants mainly containing triterpenoids as chemical constituent. The agents were effective against *Staphyllococcus aureus*. Several samples (489 samples) of *S.aureus* were isolated from healthy carriers (nose and throat) or clinical samples. Out of 489 isolates 98.6% were sensitive to trimethoprim-sulfamethoxazole. The extracted compounds from the plants were screened for antibacterial activity. *Menta vividis L.* was active against some isolates and inhibited the growth of 48.7% of the isolates.

Samy and Ignacimuthu[53] reported the antifungal activity of crude drug from the tree bark of *Terminalia arjuna* containing triterpenoid which was tested against bacteria using the hole-plate diffusion method with concentrations of 5-25 mg/mL. The effective results of bacteria were confirmed by the dilution method (1.25-2.0 mg/ml) in MIC. The results were supported by phytochemical analysis. The specific activity against pathogenic bacterium, *Bacillus subtilis* and *Staphylococcus aureus* showed the traditional usage of bark of *T. arjuna*.

Al-Hussaini *et al.*[54] extracted 20 plant leaves and screened their inhibitory effect against the rice blast pathogen. They reported that triterpenoids containing plant *Prosopis juliflora* followed by *Zizyphus jujube* significantly inhibited the mycelial growth and biomass as well as toxin production and spore germination under laboratory conditions.

Mehmood *et al.*[55] studied the antimicrobial potential of some Indian medicinal plants containing triterpenoids and their formulations. They tested twenty five different formulations based on five alcoholic extracts against several pathogenic micro-organisms. They observed that ten formulations showed higher potency compared to their constituents and good synergistic activity leading to significant reduction in the MIC values.

Ragasa *et al.*[56] extracted the air dried leaves of *Vitex negundo* which afforded vitexilactone and casticin by silica gel chromatography. Their structures were elucidated by extensive 1D and 2D NMR spectroscopy. They studied their activity and found to inhibit the growth of the fungi: *Candida albicans* and *Aspergillus niger* and the bacteria: *Staphylococcus aureus* and *Pseudomonas aeruginasa.*

Ettebong and Nwafor[57] studied the antimicrobial activities of n-hexane, chloroform, ethyl acetate and methanol extract of *Carpolobia lutea* root which were used as a folk medicine in southern Nigeria against four typed cultures of bacteria namely, *Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Bacillus subtilis* and two clinical strains of fungi, namely *Candida albicans* and *Tinea capitis* using agar well diffusion method. They reported that the ethyl acetate extract gave the widest zone of inhibition (21.0 mm) followed by chloroform when tested against *E.coli.* They also reported that none of the extracts showed any inhibitory effect against *Pseudomonas aeruginosa* and the fungal strains of *Candida albicans* and *Tinea capitis* and the most potent of these extracts was chloroform extract with Minimum Inhibitory Concentration (MIC) of 25 mg/ml for bacteria. The Phytochemical screening of the root of *C. lutea* revealed the presence of saponins, anthraquinones, flavonoids, cardiac glycosides, simple sugar and terpenes.

Horiuchi *et al.*[58] isolated the effective compound and identified it as oleanolic acid, a triterpenoid from *Salvia officinalis* (Sage) leaves and tested antimicrobial activity against vancomycin-resistant enterococci (VRE). They also tested the antimicrobial activity of similar triterpenoids, ursolic acid, uvaol, betulinic acid and betulin and found that ursolic acid also showed antimicrobial activity against VRE. The minimum inhibitory concentrations (MICs) of oleanolic acid and ursolic acid were 8 and 4 μg/ml, respectively and these two compounds also showed antimicrobial activity against *Streptococcus pneumoniae* and methicillin-resistant *Staphylococcus aureus* (MRSA). They found that these compounds also showed antibacterial activity against VRE at least for 48 h when added at concentrations that were two-times higher than their MICs.

Khan *et al.*[59] isolated amblyone, a triterpenoid from *Amorphophallus campanulatus* and studied *in vitro* antibacterial, antifungal and cytotoxic activities using disc diffusion technique and minimum inhibitory concentration was determined using serial dilution technique. They observed large zones of inhibition in disc diffusion antibacterial screening against four Gram-positive bacteria (*Bacillus subtilis, Bacillus megaterium, Staphylococcus aureus* and *Streptococcus pyogenes*) and six Gram-negative bacteria (*Escherichia coli, Shigella dysenteriae, Shigella sonnei, Shigella flexneri, Pseudomonas aeruginosa* and *Salmonella typhi*) and the MIC values against these bacteria ranged from 8 to 64 µg/ml. In antifungal screening, the compound showed small inhibition zones against *Aspergillus flavus, Aspergillus niger, Rhizopus aryzae. Candida albicans* was resistant against the compound.

Khan *et al.*[60] extracted crude from the leaves, stem bark, stem heart wood, root bark and root heart wood of *Euroschinus papuanus* and isolated fractions on partitioning with petrol, dichloromethane (D), ethyl acetate (E) and butanol (B) and studied antibacterial and antifungal activity. They observed that E fractions of the stem heart wood, D of root bark and E of root heart wood demonstrated excellent antibacterial activity and B fractions of leaves; stem heartwood and root bark demonstrated antifungal activity.

Ramesh *et al.*[61] tested the antimicrobial efficiency of aqueous, methanol, chloroform and hexane extracts of *Swertia corymbosa* containing triterpenoids and noticed maximum inhibitory activity against *Staphylococcus aureus* and *Salmonella typhi.*

Ahmad and Beg[62] extracted 45 Indian plants traditionally used in medicine using ethanol as a solvent and studied their antimicrobial activity against certain drug-resistant bacteria and a yeast *Candida albicans.* They showed that out of the 45 plants 40 plant extracts contained terpenoids and were effective antimicrobial activity against one

Smith *et al.*[63] performed a screening of eight plants from Belize for antibacterial activity. They reported that six plants showed activity against the four organisms tested. Both inoculum density and medium type played important roles in assay sensitivity.

Akinpelu[64] observed that *Anacardium occidentale* bark containing triterpenoids 60 percent methanolic extract exhibited antimicrobial activity against 13 out of 15 bacterial isolates at a concentration of 20 mg/ml.

Audu *et al.*[65], extracted components from *Ziziphus abyssinica* (root bark) containing triterpenoids using methanol, diethyl ether and cold water as solvent. They studied their activity on *Candida albicans, Escherichia coli, Salmonella* spp. and *Staphylococcus aureus* at different concentrations and found that all these components inhibited the growth of microbes.

Ramesh *et al.*[66] isolated Friedelin, epi-Friedelin, n-Octacosanol, α–Amyrin, Sitosterol, Sitosterol-3-D-glucopyranoside and luteoforol from *Bridelia crenulata* Roxb. The aqueous and methanolic extracts and their fractions were tested against ten human pathogenic bacteria and four fungal strains. They observed that inhibitory activities were maximum in the chloroform-methanol (1:1) fraction of the methanolic extract against *E.coli, K.pneumoniae* and *P.aeruginasa*, which were responsible for the pathogenesis of urinary tract infection. The above study provided scientific evidence for the efficacy of the use of *Bridelia crenulata* extracts.

Murillo-Alvarez *et al.*[67], extracted compounds from plants used in the traditional medicine of Baja California sur (Mexico) using ethanol as a solvent. They tested antimicrobial activities of the isolated compounds. The antimicrobial activity against *Bacillus subtilis, Staphylococcus aureus, Streptococcus faecalis, Candida albicans* and *Escherichia coli* were determined. *Aristolochia monticola, A.brevipes, Hymenoclea sp.* were found to be the most active.

Habtemariam and Macpherson[68] investigated the cytotoxic and antibacterial activity of an ethanol extract of leaves of a herbal drug *Eupatorium perfoliatum* containing triterpenoids. They observed that the extract showed a potent cytotoxicity and weak antibacterial activity against gram positive test organisms *Staphylococcus aureus* and *Bacillus megaterium.*

Lall *et al.*[69] observed that the water and acetone extracts of roots of *Euclea natalensis* containing triterpenoids inhibited the growth of *Bacillus cerus, Bacillus*

pumilus, Bacillus subtilis, Micrococcus kristinae and *Staphylococcus aureus* at concentration ranging between 0.1 and 6.0 mg/ml. They found that the water extract did not exert any inhibitory action on Gram-negative bacteria while the acetone extract showed inhibitory activity at a concentration of 5.0 mg/ml against all the Gram-negative bacteria investigated. The antibacterial activity of acetone extract was also investigated by a direct bioassay on TLC plates against *S. aureus*

Alves *et al.*[70] evaluated the antimicrobial, antifungal and antiadherent activity of *P sidium guajava* containing triterpenoids on oral biofilm microorganisms and oral *candidiasis in vitro*. They found that the extracts were shown to be effective in inhibiting the growth of bacteria of the oral biofilm and fungi of oral *candidiasis.*

Duraipandiyan *et al.*[71], studied the antimicrobial activity of 18 ethnomedicinal plant mostly containing triterpenoids collected from Palni hills of southern western ghats against nine bacterial strains (*Bacillus subtilis, Staphylococcus aureus, Staphylococcus epidermidis, Enterococcus faecalis, Escherichia coli, Klebsiella pneumonia, Pseudomonas aeruginosa, Ervinia sp, Proteus vulgaris*) and one fungal strain(*Candida albicans*) using paper disc diffusion method. They reported that out of 18 plants, 10 plants exhibited antimicrobial activity against one or more of the tested microorganisms at three different concentrations of 1.25, 2.5and 5 mg/disc. The study evaluated the antimicrobial activity of some ethnomedicinal plants used in folkloric medicine.

Bonjar[72] studied the antibacterial activities of the 45 species of 29 plant families used in the traditional medicine by Iranian people against *Bacillus cereus, Bacillus pumilus, Bordetella bronchiseptica, Escherichia coli, Klebsiella pneumoniae Micrococcus luteus, Pseudomonas aeruginosa, Pseudomonas fluorescens, Serratia marcescens, Staphylococcus aureus, Staphylococcus epidermidis.* He found that no plant showed activity against *Serratia marcescens* but *Bordetella bronchiseptica* were the most susceptible species. All extracts showed the same activity even after 18 months.

Saleh *et al.*[73] isolated the known triterpenoids lantic acid, camarinic acid and lantanilic acid from *Lantana camara* (L) cultivated in Egypt and carried out the antibacterial activity of lantic acid using bioautography assays for Gram-positive and Gram-negative bacteria. They found that lantic acid possess strong antibacterial activity

against *Escherichia coli* and *Bacillus cereus* in which 0.08 and 0.1 μg were the minimum inhibition doses compared to 0.05 and 0.005 μg for chloramphenicol. Their results showed that lantic acid had broad spectrum antibacterial activity.

Mathabe *et al.*[74] isolated four known compounds from the stem bark of *Spirostachys africana* using ethanol as a solvent which was used traditionally for the treatment of diarrhoea and dysentery in Limpopo province of South Africa. The isolated compounds were, two triterpenoids, compound 1 [d-Friedoolean-14-en-oic acid (3-acetyl aleuritolic acid)] and compound 2 (lupeol), and two diterpenes, compound 3[ent-2, 6alpha-hydroxy-norbeyer-1,4,15-trien-3-one (diosphenol2)] and compound 4 (ent-3beta-hydroxy-beyer-15-ene-2-one). They tested the antibacterial activity using micro dilution method and found that compound 1, exhibited MIC of 50 microg/ml against *Staphylococcus aureus, Salmonella typhi, Vibrio cholera* and *Escherichia coli* compound 2 was not active against all tested microorganisms at 200 microg/ml.

Escalante *et al.*[75] isolated three monodesmosidic triterpenoid saponins from the butanolic extract of *Phytolacca tetramera* and established their structures. They reported that the three saponins belong to the olean-type triterpenoid saponins, with 28,30 dicarboxylic groups and an olefinic double bond on C-12. They observed that phytolaccosides B and E showed antifungal activities against a panel of human pathogenic opportunistic fungi but phytolaccoside F did not show any activity. The most sensitive fungus was *Trichophyton mentagrophytes.*

Yasunaka *et al.*[76] studied the antibacterial activity of the thirty two extracts from 22 Mexican medicinal plants of 15 different families mostly containing triterpenoids against *Escherichia coli* and *Staphylococcus aureus.* They reported that seventeen plants showed antibacterial activity.All the 17 extracts except one showed higher activity against *Staphylococcus aureus* than *Escherichia coli.*

Khan *et al.*[77] extracted the leaves, seeds, stem and root barks, stem, root and heart-woods of *Michelia champaca* containing terpenoids using methanol, petrol, dichloromethane, ethyl acetate, butanol as a solvent. They observed that different fractions exhibited antibacterial activity. They also observed that fractionation drastically enhanced the level of activity particularly in the fractions of the stem bark,

dichloromethane fraction of the root bark and some fractions of the leaves.Stem and root bark extracts showed activity against some of moulds. They found that liriodenine was the active constituent of the root bark.

Aqueveque *et al.*[78] isolated a new biologically active triterpenoid favolon B from fermentation broths of *Mycena* sp. Strain 96180. They found that favolon B showed antifungal activities against *Botrytis cinerea, Mucor miehei, Paecilomyces variotii* and *Penicillium notatum*. Flavon B did not have any activities against bacteria and yeast.

Kirmizigul *et al.*[79] reported antimicrobial and antifungal activities of the MeOH extract from the flowers of *Cephalaria transsylvanica* and three triterpenic acid glycosides, transsylvanoside A-C by MeOH using an agar-disc diffusion method. They observed that both the MeOH extract and the glycosides possess antimicrobial and antifungal activities against *Staphylococcus aureus, Escherichia coli, Proteus vulgaris, Pseudomonas aeruginosa, Corynebacterium xerosis, Klebsiella pneumonia, Candida utilis, Kluyveromyces fragilis, Aspergillus oryzae* and *Aspergillus flavus* respectively.

Sudharmini and Ashalatha[80] isolated triterpenoids from *Myxopyrum smilacifolium* leaf and found the presence of ursolic acid (0.175mg/l). They reported that the triterpenoids showed antimicrobial activity against gram positive bacteria. *Candida albicans* was resistant against the compound.

Mbwambo *et al.*[81] extracted compounds from stem bark, wood and whole roots of *Ternimalia brownie* containing triterpenoids using solvents of increasing polarity, namely, pet ether, dichloromethane, dichloromethane: methanol (1:1), methanol and aqua, respectively and the extracts were tested for antifungal and antibacterial activity. They observed that the extracts of the stem bark, wood and whole roots of *T. brownii* exhibited antibacterial activity against several bacteria (*Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumonia, Salmonella typhi* and *Bacillus anthracis)* and the fungi, (*Candida albicans* and *Cryptococcus neoformans).* They found that aqueous extracts exhibited the strongest activity against both bacteria and fungi.

Jacinda *et al.*[82] extracted large quantities of pentacyclic triterpenoids, saponin collectively known as Centelloids. These terpenoids include Asiaticoside, Centelloside,

madecassoside, Brahmode etc. *In Planta,* the *Centella* triterpenoids can be regarded as phytoanticipins due to the antimicrobial activity and protective role against attempted pathogen infection.

Sharma *et al.*[83] reported that ingestion of *Lantana camara* foliage by grazing animalscauses intrahepatic cholestatis and amociated liver damage. The hepatotoxins were pentacyclic triterpenoides called Lantadenes.A number of biological activities have been associated with various parts of *Lantana* in folk medicine.Roots of Lantana plants were rich in oleanolic acid, a heteroprotective triterpenoid.Pentacyclic triterpenoids were the focus of attention for drug research for anti-cancer, anti-AIDS, anti inflammatory and anti microbial activities.

Rajenderan *et al.*[84] isolated pentacyclic triterpenoids, namely Ursolic acid, 2-hydroxy ursolic acid, (Asiatic acid, glycerol-1,2-dilinolexyl-3-o-b-D-galactopyronose from the methanolic extract of leaves of *M. malabathricum*.This plant was selected as one of the most promising source of antimicrobial agents.It showed anti-viral,cytotoxic, anti-oxidant, anti-cancer activity,anti-hypertensive activity,anti-inflammatory and anti-pyretic properties.

Chaudhury *et al.*[85] showed that the phytochemicals betulinic acid (a), wogonin (b) and oroxindin (c) isolated from the aerial parts of *Bacopa monnieri* and *Holmskioldia sanguinea* showed significant antifungal activity against the two fungi *Alternaria alternata* and *Fusarium fusiformis*. Inhibition of root growth germination of wheat seeds was observed for all three compounds which showed 100% inhibition at 10 micro g/mL. Compounds (a) and (b) showed potent inhibition of *Alternaria alternata* compared with oroxindin at a concentration of 4 micro g/mL, whereas compound (b) was an effective inhibitor of both fungi.

Ghosh *et al.*[86] isolated of two triterpenoids betulinic acid and lupeol from the leaf extract of *Psidium guajava* and their potential antimicrobial and phytotoxic activities. All the structures of the isolated compounds were confirmed by spectral (IR, NMR) analysis and by comparison with the literature reports available.

Betulinic acid is a naturally occurring pentacyclic triterpenoid and has been shown to exhibit a variety of biological activities including inhibition of human

immunodeficiency virus (HIV), antibacterial, antimalarial, antiinflammatory, antithelmintic and antioxidant properties reported by Yogeeswari.*et al.*[87].

Shafi *et al.*[88] reported that the Leaves of two plants, *a* terpenoid fraction of both plants showed significant antifungal activity against *F. equiseti, C. gloeosporioides* and *A. alternata* when tested by spore germination method. MIC values of terpenoid fraction of *D. stramonium* extract were 0.05mg/ml against *F. equiseti,* 0.1mg/ml against *C. gloeosporioides* and 0.5mg/ml against *A. alternata* when tested by disc diffusion method. Similarly, the MIC of *C. mucronata* leaf extract against *F. equiseti* was found to be 0.01 mg /ml. The MIC value of *D. stramonium* leaf extract (terpenoid fraction) was 0.5mg/ml against *A. alternata.*

One plant extract (*Datura*) containing triterpenoids was subjected to column separation. The separated fractions were tested against *F. equiseti* and *C. gloeosporioides* following spore germination bioassay. Potential fractions (fraction 6-20 & fraction 26-35) were also tested by disc diffusion bioassay. Combined column fractions (6- 20) could inhibit the growth of *C. gloeosporioides* at a concentration of 0.2mg/ml. Another column fraction (26–35) could check the spore germination of the *F. equiseti* at a concentration of 0.08mg/ml reported by Barre *et al.*[89].

Ahmed *et al.*[90] screened antifungal compounds (terpenoids) from the roots of the wild carrot, *Daucus carota* L. ssp. *carota* (Apiaceae) and it was found to contain a range of antifungal activity against *Fusarium oxysporum* and *Aspergillus niger.*

Barrero *et al.*[91] reported that *a* wide spectrum of secondary metabolites such as phenols, flavonoids, quinones, tannins, essential oils, terpenoids, alkaloids, saponins and sterols which showed antimicrobial activity. The compounds were isolated from higher plants. They investigated antifungal efficacy of sesquiterpene lactones isolated from the six *Centaurea* species (*C. bombycina* Boiss ex D.C., *C. granatensis* Boiss, *C. monticola* Boiss, *C. incana* Desf., *C. maroccana* Ball. and *C. sulphurea* Willd.) against the fungus *Cunninghamella echinulata.* They reported that the two compounds costunolide and dehydrocostunolide, were responsible for the antifungal activity.

Scher *et al.*[92] prepared a dichloromethane and a methanol extract of the liverwort *Bazzania trilobata* (L.) S.F. Gray (Lepidoziaceae) and showed their antifungal

activity against some phytopathogenic fungi (*Botrytis cinerea, Cladosporium cucumerinum, Phythophthora infestans, Pyricularia oryzae* and *Septoria tritici)* due to the presence of terpenoids. From the extracts they isolated six antifungal sesquiterpenes: 5-and 7-hydroxycalamenene, drimenol, drimenal, viridiflorol, gymnomitrol and chloroisopiagiochin.

Digrak *et al.*[93] showed that compound extracted from *Terminalia arjuna* containing triterpenoids was found to be effective against *F.equiseti* and other two pathogens.The leaf extract of *Clerodendrum viscosum* could completely check the radial growth of the test fungi.

A mixture of loliolide 1 (>85%) and paniculatadiol 2 (<15%) was obtained from the ethyl acetate leaf extract of *Pterocarpus indicus* by silica gel chromatography, while the air-dried flowers afforded lupeol 3 and phytol esters 4. The structures of **1-4** were determined by NMR spectroscopy. Antimicrobial tests on a mixture of **1** and **2** indicated that it has moderate activity against *Candida albicans* and low activity against *Pseudomonas aeruginosa, Escherichia coli,* and *Aspergillus niger.* It was found inactive against *Staphylococcus aureus, Bacillus subtilis,* and *Trichophyton mentagrophytes* reported by Ragasa *et al.*[94]

Parveen *et al.*[95] reported that the methanolic extract of the leaves of *Peltophorum vogelianum* (Caesalpiniaceae) afforded a new phytoconstituent, 2-methoxy-4,5-dihydroxy-1(7,8-dihydroxyethylene)-8-β-D-glucuropyranoside named as peltophorumyl-β-D-glucuropyranoside (**e**), along with four known phytoconstituents, 1-pentatriacontanol (**a**), friedelin (**b**), β-sitosterol (**c**) and β-sitosterol-β-D-glucopyranoside (**d**). The structures were established on the basis of chemical and physical evidence (IR, ^{1}H-NMR, ^{13}C-NMR, DEPT, HSQC, HMBC and MS). Moreover, Compound **5** showed significant antimicrobial activity.

Ramesh *et al.*[96] made various extracts of the leaves of *Begonia malabarica* Lam. (Begoniaceae). From the extracts of six known compounds, (viz. friedelin, epi-friedelinol, beta-sitosterol, luteolin, quercetin and beta-sitosterol-3-beta-D-glucopyranoside) were isolated. The aqueous and organic solvent extracts were also tested against ten human pathogenic bacteria and four fungal strains by the agar-well

diffusion method. All the extracts were devoid of antifungal activity against the tested fungi.

Duraipandiyan *et al.*[97] designed an experiment to evaluate the antifungal activity of *Azima tetracantha* extracts and isolated compound (friedelin) against fungi. They fractionated the extract through silica gel column. The antifungal activity of *Azima tetracantha* crude extracts and isolated compound (friedelin) were evaluated using the micro dilution method. Hexane extract showed some antifungal activity. The lowest MIC against *Trichophyton rubrum* was 62.5 µg/ml and the MIC against *Curvularia lunata* was 62.5 µg/ml.

Shing *et al.*[98] reported that the hexane extract of *Heliotropium marifolium* yielded a mixture of triterpenoids: β-sitosterol, stigmasterol, β-amyrin, friedelan-3β-ol (epifriedelenol), cycloartenone, β-amyrin acetate, friedelin and epifriedenyl acetate. Their Isolated triterpenoid and reference antibiotics (gentamycin/mycostatin) were tested against selected pathogenic bacteria and fungi, e.g. *Escherichia coli, Staphylococcus aureus, Aspergillus niger* and *Penicillium chrysogenum*. The inhibition zone (IZ) and the activity index (AI) of isolated compounds were recorded. They reported that epifriedenyl acetate (IZ = 17; AI = 1.06) was most active.

Joseph *et al.*[99] reported that the 50% methylene chloride in hexane fraction (column fraction of the extract of leaves of *Ficcus racemosa*) showed antifungal activity.. The extract inhibited the growth of several plant pathogens (*Curvularia sp, Colletotrichum gloeosporioides, Alternaria sp* and *Fusarium sp).*

Siddiqui *et al.*[100] isolated a new pentacyclic triterpene, oleanderol and the known betulin, betulinic acid, ursolic acid and oleanolic acid from the leaves of *Nerium oleander*.The structure elucidation of oleanderol and identification of betulin,betulinic acid, ursolic acid and oleanolic acid had been carried out through chemical and spec tral studies.They had antimicrobial properties also.

From the above literature, the present work were designed.Several compounds were isolated and derieved. All the compounds were tested for antimicrobial activities. In the following chapters the process of the isolation, preparation of derivatives and their bioassay have been discussed in details.

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