The work is divided in to two parts

a. Utilization of terpenoids and allied molecules for value added products

b. Comparative study of colchicine bearing plants

PART-A

Title:
Utilization of terpenoids and allied molecules for value added products

Introduction:
Essential oils (Eos) which were once considered inactive waste products of plant metabolism and have no significant biological function, are now being realized for their importance as a means of chemical communication which the plants keep itself against competitors, predator and pathogens. The term ‘essential oil’ is thought to derive from the name coined in the 16th century by the Swiss reformer of medicine, Paracelsus von Hohenheim; he named the effective component of a drug “Quinta essentia”. Essential oils and their components are reported to have antimycotic, antitoxigenic, and insecticidal properties. In traditional system of medicine the role of essential oil bearing plants was taken as the most effective part of the herbal drugs. With the passage of time its identity as having medicinal properties, got diverted to aromatic science.

Objective:
Terpenoids are widely used as perfumery agents but need some kind of attention to improve market value by simple cost cutting techniques to give value added products. Since there is an injustice with the terpenoids, their utility as bioactive molecules is yet to be properly explored.

1. Mentha waste as a source of value added products

*Mentha piperita*, a commercially important medicinal plant, yields essential oil finding ample use in cosmetics, liquor, confectionary, pharmaceutical and related industries. *M. piperita* after steam distillation gives bottom pitch and high boiling hydrosol as waste products. The bottom pitch waste is inexpensive and finds use as an adulterant to perfumed incense sticks. The present investigation has shown that the so called bottom pitch contain important product like 3-octanol, menthols and are
hooked to long chain fatty acids as esters and also serves as fixative to other non hooked terpenoids.

**Results and Discussion**

GC-MS data of high boiling hydrosol after saponification showed maximum concentration of menthone, whereas bottom pitch showed menthone in appreciable quantities. The GC data showed presence of oleic and palmitic acid in appreciable amounts after saponification of the waste material.

**Experimental**

The present work comprises of removal of long chain fatty acids by saponification, identification of fatty acids as their methyl ester and isolation of constituents thus obtained by using hydrodistillation, solvents of different polarity for extraction and characterization using GC-MS and GC-FID.

**2. High yielding synthesis of ω- acetyl longifolene**

Longifolene, C_{15}H_{24} (Decahydro-4, 8, 8-trimethyl-9-methylene-1-4-methanoazulene), a tricyclic sesqui-terpene hydrocarbon, is commercially important chemical and is used in perfumery industry owing to the woody odor of its chemically modified forms.

**Results and discussion**

Though acetyl longifolene is being prepared commercially prepared by different methods but all the processes are not economically viable due to poor yield thus it was taken as a challenge to to establish a potent method with very high yield of 55-70% against industrial methods where yield lies between 5-15%. Longifolene was converted in to acetyl longifolene in traces using different catalyst such as BF₃, ZnCl₂, AlCl₃, PPA. GC chromatogram showed geometrical isomers of acetyl longifolene (Z and E) at RT 19.99, 21.98 in the ratio ~25:40 and both are valuable products for perfumery industry. The yield with all the catalysts was very low except FeCl₃ under appropriate conditions with which acetyl longifolene was obtained in very good yield of 55-70%. The formation of acetyl longifolene was characterized by ^1H NMR and GC-MS.
ABSTRACT

Experimental

Scheme

\[
\text{longifolene} \xrightarrow{\text{a.b.c}} \text{acetyl longifolene} + \text{E-Z isolinigfolene}
\]

\(a=\text{Lewis acid, } b=\text{acetic anhydride/ acetyl chloride, } c=\text{dichloromethane, } \sim 25:40\)

3. Extraction and characterization of Kinnow peels oil from North-West region

Introduction
Kinnow is a hybrid of two citrus cultivars *Citrus nobilis* X *Citrus deliciosa* and its peel is a waste product. *d-limonene* a monocyclic monoterpene, obtained from the steam distillation of Kinnow peels is a major constituent in several citrus oils (orange, lemon, mandarin, lime, and grapefruit) & turpentine oil.

Results and Discussion
The results concluded that Kinnow peels contain maximum concentration of *d-limonene* (a valuable terpenoid) in the month of Jan.-April. Limonene has gained much importance now a day because of its utilization in various households and it is also used as a solvent. So it is worth to find out the concentration of limonene in Kinnow peels.

Experimental
The citrus peels were collected in its peak season of Feb-March continuously for 2 years (2010-2011) and were subjected to hydrodistillation. The GC-MS showed more than 90% concentration of *d-limonene* in oil.

4. An efficient synthesis of menthofuran and menthofuran lactone, powerful perfumery agents

Introduction
Menthofuran is basically obtained from flower buds of peppermint plants. It is widely used as an perfumery agent and is extremely expensive.
ABSTRACT

Results and Discussion
Menthofuran is widely used as a perfumery material. The present investigation reports an efficient, inexpensive and high yielding method for the synthesis of menthofuran and menthofuran lactone. The characterization was done using GC-MS. The yield of menthofuran and menthofuran lactone is 40-50%. Ho et al. in 1980, reported the synthesis of menthofuran from isopulegole via isopulegole epoxide followed by oxidation and cyclodehydration. It is interesting to note that a mixture of menthofuran and menthofuran lactone gives more acceptable fragrance and has persistency in fragrance than menthofuran.

Experimental

Scheme

Citronellal was used as the starting material for the synthesis of menthofuran and menthofuran lactone.

5. Antimalarial and antioxidant potential of Meldrum’s acid analogues (a pseudo hemiterpenoid)

Introduction
Meldrum’s acid analogues are reported as the key intermediates for cycloaddition reactions and for the synthesis of heterocyclic compounds of biological importance such as cardiotonic and HIV integrase inhibitory activities. They are also reported to serve as the versatile substrates for various kinds of reactions.

Results and Discussion
The synthesized compounds were evaluated for antimalarial (against P. falciparum) and free radical (DPPH and ABTS) scavenging activities. Five compounds were
found to be most active against the resistant strain of *P. falciparum* with IC\(_{50}\) ranging from 9.68-16.11μM.

Compounds 18 l, 18m, and 18n were found to be strong free radical scavengers with 76.0%, 66.1%, and 40.2% respectively scavenging of the DPPH activity. Compounds 18 l, 18m and 18n showed the 92.5%, 95.5%, and 52.7% respectively scavenging of the ABTS free radical.

**Experimental**

A new methodology for the synthesis of arylidene analogues of Meldrum’s acid has been developed and follow. 24 compounds were synthesized and evaluated for antimalarial and antioxidant activity.

Reagents and conditions: (i) For 18a and 18d–18x: MeOH, rt, 15–45 min, 85–96% and for 18b and 18c: MeOH, 3 Å MS, reflux, 3 h, 77–81%.
6. Synthesis and characterization of propiophenone analogues of acetyl carene

Carene or $\Delta^3$-carene, is a bicyclic monoterpene which occurs naturally as a constituent of turpentine, due to its pungent odor, carene remains a waste material as it has no use from medicinal chemistry point of view but still there is a scope for its chemical modifications for medicinal as well as perfumery products. It is a valuable synthone as it contains a cyclopropane ring like ciprofloxacin. The present work involves utilization of easily available synthones as a source for potent bioactive molecules.

**Results and Discussion**

The reaction was tried with an array of reagents such as HCl/dioxane, methanol/NaOH CH$_3$COOH/H$_2$SO$_4$, NaH/THF. Since it contains an important moiety in the form of dimethyl cyclopropane systems which have tendency to open The reaction was succeeded in NaH/THF. The reaction products were characterized by NMR, Mass and IR. The product obtained was an oil. As such 5 propiophenone derivatives were synthesized.
Experimental

\[
\begin{align*}
\text{carene} & \xrightarrow{a} \text{acetyl carene} \\
\end{align*}
\]

Propiophenone derivatives of carene

\[ \text{Propiophenone derivatives of carene} \]

a= acetylchloride\(\text{ZnCl}_2\), b= dioxane/H\(\text{Cl}\), c= acetic acid/H\(\text{2SO}_4\), d= methanol/NaOH, e= NaH/THF,
f= substituted aldehydes

\[
\begin{align*}
\text{2,4,5-Trimethoxybenzaldehyde} & \quad \text{2,5-dimethoxy benzaldehyde} \\
\text{3,4,5-trimethoxy benzaldehyde} & \quad \text{2,3-dimethoxy benzaldehyde} \\
\end{align*}
\]

7. Modification of monoterpenoids into potential antitussive agents.

Introduction

Menthol and camphor, monoterpenoids are known collectively as volatile or aromatic oils, which have been widely used in the symptomatic treatment of upper respiratory tract infections.

Results and Discussion

Lactams of menthol after conversion to menthone and camphor were synthesized and were found to show better antitussive activity than menthol and camphor. Guinea pigs were used for antitussive activity. Perspex chamber with nebulizer was used for whole activity.
ABSTRACT

Experimental

\[ \text{OH} \xrightarrow{a} \text{O} \xrightarrow{b} \text{NOH} \xrightarrow{c} \text{NH} \]

a) CrO$_3$/H$_2$SO$_4$, acetone b) NH$_2$OH.HCl/NaOH, methanol c) C$_6$H$_5$SO$_2$Cl/NaOH, THF

Menthone and camphor lactams were synthesized from their oximes involving Beckmann rearrangement

8. Synthesis of propiophenones and their corresponding pyrazole analogues as potential bioactive agents

Introduction

Propiophenone derivatives or chalcones have been reported to exhibit a variety of biological activities such as antibacterial, antifungal, antitumor and anti-inflammatory properties. Pyrazoles have a long history of application in agrochemicals and pharmaceutical industry as herbicides and active pharmaceuticals.

Results and Discussion

The present work involves synthesis of propiophenone analogues and further converted into corresponding pyrazoles

Reagents and conditions: (i) 5% NaOH, ethanol, rt, 1 h, (ii) NH$_2$NH$_2$.H$_2$O, CH$_3$COOH, reflux, 4 h.
ABSTRACT

Compound 4, 12 and 26 showed broad spectrum of cytotoxicity against four cell lines. Compound 26 was found to be the most potent with inhibition

As such 23 compounds were synthesized and evaluated for cytotoxic and antimicrobial activity. Compound 4, 12 and 26 ranging from 70-75% against all four different cell lines. Compounds 4, 12 and 23 were found to possess significant antimicrobial activity among all tested compounds with an MIC value ranging from 1.9 to 31.2 μg/ml against the various microbial strains employed.

Experimental

The compounds were evaluated for cytotoxic activity against four cell lines viz. PC-3, OVCAR, IMR-32, HEP-2. The synthetics were also evaluated for antimicrobial activity against six reference bacterial strains; S. aureus, (MTCC 96), B. subtilis (MTCC 2451), P. aerogenosa (MTCC 2642), E. coli (MTCC 82), S. typhimurium (MTCC 1251), P. acne and antifungal potential were assessed against A. niger (MTCC 1344) and C. albicans (MTCC 3018). The compounds were characterized by IR, NMR, Mass.
PART-B

Title:
Comparative study of colchicine bearing plants

Introduction
Colchicine a toxic natural product and secondary metabolite, originally extracted from plants of the genus *Colchicum* (Autumn crocus, *Colchicum autumnale*, also known as “meadow saffron”). It is used for treatment of gout and also as an anti-inflammatory agent.

Aim of work
Literature survey revealed that *I. indica* seeds contained maximum concentration of colchicine. However no data on *I. indica* corms have been reported yet. So it is worth to find out the concentration of colchicine in corms using sensitive techniques. However there was no literature reported on comparative data of different colchicine bearing plants. So the study confined to the estimation of colchicine in corms of different colchicine bearing plants.

Results and Discussion
Plants selected (Corms) for comparative studies were *C. luteum, G. superba* and *I. indica* and the techniques used for quantification are HPLC and HPTLC. Different extracts were prepared and were compared and validated using HPLC and HPTLC. HPLC and HPTLC data showed maximum concentration of colchicine in *C. luteum*, sonication extract i. e. 0.19 and 0.16% resp.

Overlay chromatogram of colchicine using HPLC
Experimental
Plants were subjected for extraction techniques such as Soxhlet, percolation and sonication using CHCl₃ as a solvent. HPLC method was optimized using different concentrations of mobile phase and different flow rate. Mobile phase combination of ethyl acetate: ethanol: formic acid (9: 1: 0.01 v/v/v) was found to be most suitable. Best resolution and sensitivity of the method for colchicine was detected at 352 nm.

A mobile phase consisting of ethyl acetate: ethanol: formic acid in ratio of 9:1:0.01 v/v/v was used for the analysis which gave sharp and well resolved peak of colchicine. Best resolution and sensitivity of the method was obtained at 352 nm with retention factor of 0.15.