Texila International Journal of Public Health
Special Issue-2025
DOI: 10.21522/TIJPH.2013.SE.25.01.Art022

Phytochemical Analysis of Trikatu (Thirukadugam): A Study through Gas Chromatography and Mass Spectrometry

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Abstract

Trikatu (Thirukadugam) is an amalgamation of various herbal parts which is using in traditional medicinal system like siddha, Ayurvedha, Homeopathy etc. This formulation is effective in respiratory problem acts as bronchodilator and expectorants. It enhances the digestive juice secretion and increase the appetite. Antiobesity property regulate the serum cholesterol and triglycerides level. Hence it might increase sensitivity of insulin receptor and its phytochemical component acts as bio enhancers to promote antidiabetic properties. It is utilized to treat the arthritis, gout disease and good detoxifier agent. Although preceding report shows Trikatu has potential for therapies, phytochemical component is not well determined. This evokes us to initiate the present study, the ethanolic extract of Trikatu is subjected to phytochemical screening the following compounds like alkaloids, sterols, glycosides, saponins, carbohydrates, flavonoids, tannins and proteins has been present. Bioactive components were identified specifically, Amoxapine, 4,2'-Dihydroxychalcone,Succinic acid, Glycosides, 2,5-Cyclohexadiene-1,4-dione, 2,5-bis(1,1-dimethylpropyl)-, Synephrine, Sotalol, Dyphylline, Amrinone and Benzene, 3-[3-iodo-2-(iodomethyl)-2-methylpropyl]-1,2,4,5-tetramethyl—. These components might establish pharmacological nature and therapeutic potentials of the herbal extract.

Keywords: *Amoxapine, Amrinone and Benzene, phytochemical component, Trikatu (Thirukadugam).*

Introduction

Herbal medicine means plant-derived medicines that has been practiced for quite a long time. World Health Organization (WHO) report stated that more than 70% of the world's population uses herbal medicines, especially in underdeveloped and developing countries. Even developed countries from Europe like Germany and France have prescribed herbal extracts as drugs. Herbal medicine treatment possesses a holistic approach to the disease. The task of herbal medicine in treatment not only suppress the causes of disease, rather it ameliorates many ill effects that resulted in a disease [1]. Herbal medicine users are frequently undergoing treatment for chronic diseases than acute diseases and engage in both physical and preventive health behaviors. Common cold/flu infections, respiratory problems, and gastrointestinal diseases are health issues that are effectively cured by herbal formulations [2]. In OSCC and severe oral epithelial dysplasia, salivary MMP-9 levels are

Received: 12.01.2025 ***Accepted: 27.01.2025*** ***Published on: 31.01.2025***

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markedly raised, indicating that it may be a signal for malignant transformation [3].

Thirikadugam is a polyherbal formulation with a combination of three components *Piper nigrum*, *Piper longum* and *Zingiber officinale* in the ratio of 1:1:1. It is mainly effective in diminution of symptoms for respiratory ailments and also acts as a bronchodilator [4]. From literature reports, it is evident that Trikatu has antihyperlipidemic potential and physiological activities of the liver, pancreas and spleen have been enhanced on consuming it. Perhaps improving liver functions, Trikatu acts as hepatoprotective activity [5, 6]. One of the components of the formulation, *Zingiber officinale* has antidiabetic, anti-inflammatory, and neuroprotective properties [7]. Also, the characteristics of Piper nigrum have also been investigated which revealed that it possesses antithyroid, antioxidant, dyslipidemia, lipid-lowering, and anti-amoebic properties [9, 10]. *Piper longum* has the many therapeutic potentials like anti-inflammatory, anti-obesity, ant—helminthic and immunomodulatory properties [11, 12]. There is a negative correlation between salivary 1-25dihydroxycholecalciferol and IL-17A levels during orthodontic treatment phases, indicating that vitamin D administration may hasten tooth movement while minimizing tissue injury [8].

All these therapeutic potentials of Trikatu may be attributed to the presence of its phytochemical components which are not yet found out thoroughly. In the present study the ethanolic extract of thirikadugam was subjected for phytochemical analysis followed by quantitative determination of organic compounds by Gas chromatogram mass spectrometric method (GCMS). The identification by NGS analysis of different genetic changes across grades of oral squamous cell carcinoma advances limited intervention options and allows for personalized therapeutic planning [13]. *Zingiber officinale* exhibits high phenolic and flavonoid content which gives a good antioxidant nature to the formulation. Flavonoids possesses rich anti-diabetic properties [14]. Alkaloids of *Piper nigrum* and *Piper longum* manage the glucose homeostasis by reducing the blood glucose level in diabetic conditions [15, 16] By causing apoptosis, preventing glycolysis, and lowering migration and invasion in HSC-3 oral cancer cells, calotropin demonstrates anti-cancer potential [17].

These bioactive components play a vital role in the treatment of different diseases. More quantity of bioactive components in herbs are good antioxidants, in which the free radicals are reduced in the cells further prevents lipid peroxidation which possess treatment to various diseases and aging conditions. Anti-inflammatory effects of the bioactive components that are essential to prevent progressive aggravating of certain conditions like diabetic complications, arthritis, other musculoskeletal disorders and even manage pain. β-Sitosterol exhibits promise as a treatment for oral cancer by controlling apoptotic signaling and producing cytotoxic effects [18]. Anti-hyperlipidemic effects normalise the lipid level in blood and various organs. Hyperlipidemia causes non-communicable diseases like obesity, hypertension and cardiac failure. Dyslipidemia has been caused by lifestyle modification are the key elements for the development of obesity and type II diabetes mellitus. A plaque ecology that favors *Streptococcus mutans*, increased DMFT scores, and increased caries severity are all associated with *H. pylori* in cavitated carious lesions [19]. Since the bioactive compounds of Trikatu has not been reported so far, the present study planned to investigate the individual phytochemical and bioactive compounds by gas chromatography mass spectrometric analysis.

Preparation of Extract

Equal quantities of all the three herbs, dried fruits of *Piper longum* Linn. (Long Pepper), *Piper nigrum* (Black Pepper), and dried rhizomes of *Zingiber officinale (dry* ginger*)* are

finely ground separately in a mortar pestle. Individual fine powders are mixed properly after weighed in equal quantity. The resulting fine powder, which has additional therapeutic efficacy due to its larger surface area, is obtained by sieving this mixture of powders using sieve no. 80. Next, the finely ground Trikatu powder is kept dry in airtight containers.

Preparation of Ethanolic Extract

100g of Trikatu churna and its ingredients were extracted in 95% ethanol at 50 - 60°C in a soxhlet apparatus separately. The extract was concentrated to dryness in rotatory evaporator (50 -60°C).

Phytochemical Analysis

The ethanol extract of the plant was tested for the presence of various bioactive compounds.

Test for flavonoid: To 1 ml of the extract, a few drops of 1% NH3 was added in a test tube. An intense yellow colour was produced indicating the presence of flavonoid compounds.

Test for tannins: To 1 ml of extract, 2 ml of 5% FeCl3 was added. The formation of blue-black precipitate indicated the presence of tannins.

Test for alkaloids: 1 ml of the extract was stirred with 2 ml of 2N hydrochloric acid and Mayer's reagent (Potassium mercuric iodide solution) was added to it. A white turbid precipitate was formed showing the presence of alkaloids.

Test for glycosides: To 1 ml of extract, 1 ml concentrated sulphuric acid (H_2SO_4) was added. After hydrolysis of the test solution, Fehling's solution was added. A black, red precipitate was formed indicating the presence of glycosides.

Test for terpenoids: 2 ml of extract was dissolved in 2 ml of chloroform and evaporated to dryness. 2 ml of concentrated H_2SO_4 was carefully added to the mixture to form a layer. An interface with reddish brown coloration was formed indicating the presence of terpenoids.

Test for saponins: Honeycomb test- 1 ml of extract was taken in a test tube and few drops of 5% sodium bicarbonate solution was added. The mixture was shaken vigorously and kept for 3 min. Formation of honeycomb-like froth shows the presence of saponins.

Test for steroids: 2 ml of extract was dissolved in 2 ml of chloroform and 2 ml of concentrated H2SO4 was added along the sides of the test tube. The upper layer turned red and H2SO4 layer showed yellow colour with green fluorescence indicating the presence of steroids.

Test for carbohydrates: To 1 ml of extract, 5 ml of Benedict's reagent was added and boiled for 5 minutes. Formation of bluish green colour showed the presence of carbohydrates. When this was boiled for few minutes more, a reddish pink colour was formed indicating the presence of flavonoid.

Detection of proteins and amino acids: The extracts were treated with few drops of concentrated Nitric acid solution. The formation of a yellow colour indicates the presence of proteins.

GC-MS Analysis

Gas chromatography is the ability to separate the chemical components in a sample based on the volatile nature of each component and MS individual characterization of the components are done depending on their charge and molecular weight. GC-MS analysis is a minute quantity of ethanol extract, phytochemical analysis of Trikatu was carried out by using a Perkin Elmer Clarus SQ8C instrument. DB-5 MS capillary standard non-polar column of length 30 meters was used. Helium was used as carrier gas at a flow rate of 1ml/min. The injection of the sample was 1 microlitre and the injection temperature was 250°C, the oven temperature is maintained at 280 °C. The course to 550 Da.

Identification of compound retention indices was performed by correlating to the retention

times of series. Each component was pointed out by matching of its retention with either with authentic compounds or with literature data. By using the details in National institute standard and technology (NIST) which contains 62,000 patterns the examination of Mass spectrum report was begun.

The unknown components spectrum was compared with the spectrum of revealed components stored in the NIST library. The name, molecular formula, molecular weight and chemical structure of the components of the test materials of increasing in oven temperature from 110 °C (isothermal for 2 min) with an increase of 10 °C /min to 200°C /min then 5°C /min to 280°C /min ending with a 9 min, isothermal at 280°C. The mass spectrum was taken at 70 eV, a scan-interval of 0.5 sec, and fragments from 40 were found out.

Results

In ethanolic extract of Trikatu, the following phytochemical constituents like Alkaloids, Sterols, Glycosides, Saponins, Carbohydrates, Flavonoids, Tannins and Proteins were identified. Gas mass sepectetmetric analysis revealed the presence of Amoxapine, 4,2'-Dihydroxychalcone, Succinic acid, Glycosides, 2,5-Cyclohexadiene-1,4-dione, 2,5-bis(1,1-dimethylpropyl)-, Synephrine, Sotalol, Dyphylline, Amrinone and Benzene, 3-[3-iodo-2-(iodomethyl)-2-methylpropyl]-1,2,4,5-tetramethyl— (Table 1 and Table 2) (Figure 1 to 10).

Table 1. Phytochemical Component in the Ethanolic Extract of Trikatu (Thirikadukam)

S. No	Phytochemical component	Ethanol extract of Trikatu
1	Alkaloids	**Present**
2	Sterols	**Present**
3	Terpenoids	**Present**
4	Glycosides	**Present**
5	Saponins	**Present**
6	Carbohydrates	**Present**
7	Flavonoids	**Present**
8	Tannins	**Present**
9.	Proteins	**Present**

Table 2. Bioactive Compounds in Trikatu (Thirukadugam) are Determined by using Gas Chromatography Mass Spectrometry

S.No	Name of the compound	Compound nature	Molecular formula	Molecular weight	Therapeutic use
1	Amoxapine	N-demethylated benzene	$C_{17}H_{16}ClN_3O$	313.781	Antidepressant
2	4,2'-Dihydroxychalcone	Flavanoids	C15H12O3	240.25	Anti-cancer agents.
3	Succinic acid	dicarboxylic acid	$C_4H_6O_4$	118.0880	Antidiabetic property
4	2,5-Cyclohexadiene-1,4-dione, 2,5-bis(1,1-dimethylpropyl)-	Phenolic compound	C16H24O2	248.37	Antimicrobial activity, antioxidant activity.

5	Synephrine	Alkaloids	$C_9H_{13}NO_2$	167.20	Antiobesity, anti diabetic activity by suppress glucose production, increased peripheral utilization of glucose
6	Sotalol	Phenylsulfonamide	C12H21ClN2O3S	272.37	Prevent drug arrhythmias
7	Dyphylline,	Oxopurine	C10 H14 N4 O4	254.24	Bronchodilator for asthma
8	Amrinone	Pyridine derivative	$C_{10}H_9N_3O$	187.20	Positive iontrophic effect and vasodilator
9	Benzene, 3-[3-iodo-2-(iodomethyl)-2-methylpropyl]-1,2,4,5-tetramethyl—		$C_{15}H_{22}I_2$	456.14400	Antitumor and anticancer activity

Amoxapine brings down norepinephrine uptake and intensifies the level of norepinephrine in heart and telencephalon through facilitating the sympathetic activity and acts as antidepressant level [20]. 4,2'-Dihydroxychalcone- acts as an anticancer agent, improves glycogen content in different organs, and is effective to treat metabolic disturbances in Diabetis mellitus. Dihydroxychalcone and its derivative causes reduction in the glycogen content in liver but causes changes in brain and spinal cord glycogen contents. Antioxidant activity properties of Dihydroxychalcone suppresses the symptoms of diabetes. miRNA 21, miRNA 184, and miRNA 145 are circulating exosomal miRNAs that exhibit promise as plasma biomarkers for identifying individuals with leukoplakia, OSMF, and OSCC who are at high risk of developing malignant transformation [21].

Flavonoids possess the antidiabetic potential and are effective in normalising the metabolic disturbances in Diabetes mellitus. Chalcones too acts as anticancer agents [22, 23]. Ester of Succinic acid has potent insulinotropic effect that increases the insulin secretions in pancreas and decreases the insulin resistance in target cells. These effects control the blood glucose level leading to prevention of complications in Diabetes mellitus [24, 25]. 2,5-Cyclohexadiene-1,4-dione, 2,5-bis(1,1-dimethylpropyl)- present in various plant extracts is an effective in antimicrobial agent and posseses antioxidant and anti-inflammatory activity by inhibiting the cyclooxygenases-2 [26]. In OPMDs, miRNAs are essential because they have the potential to be both therapeutic targets and diagnostic indicators [27].

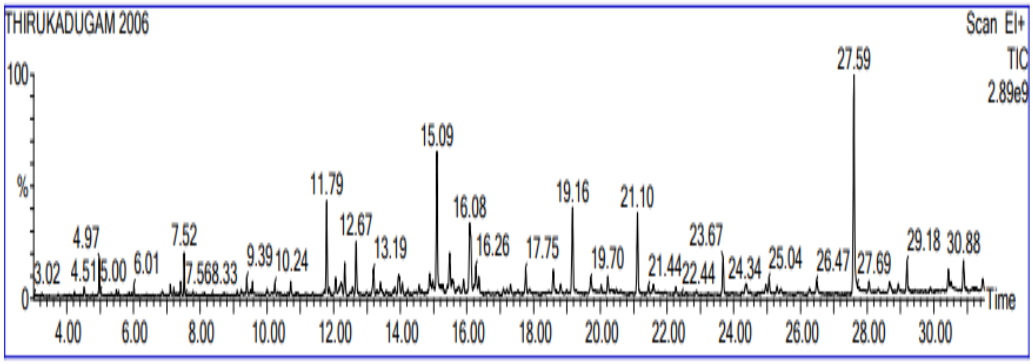


Figure 1

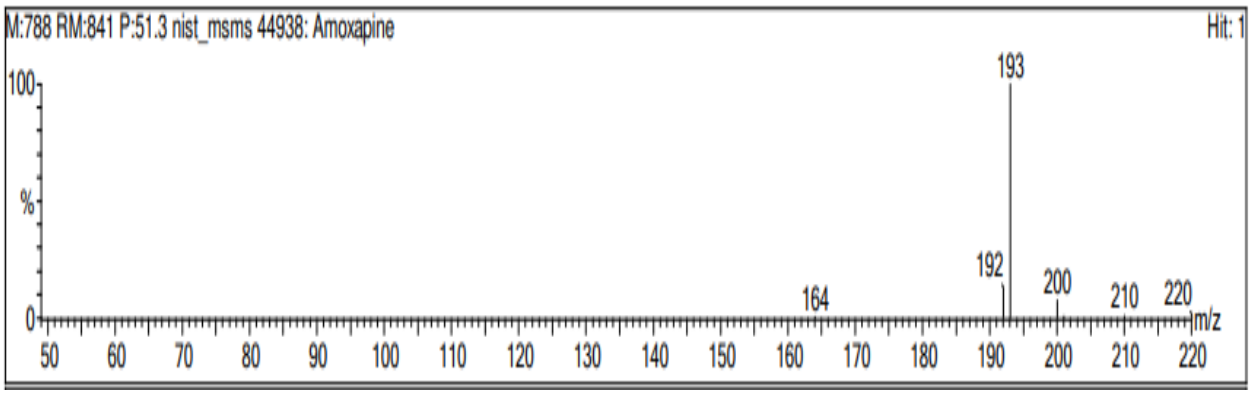
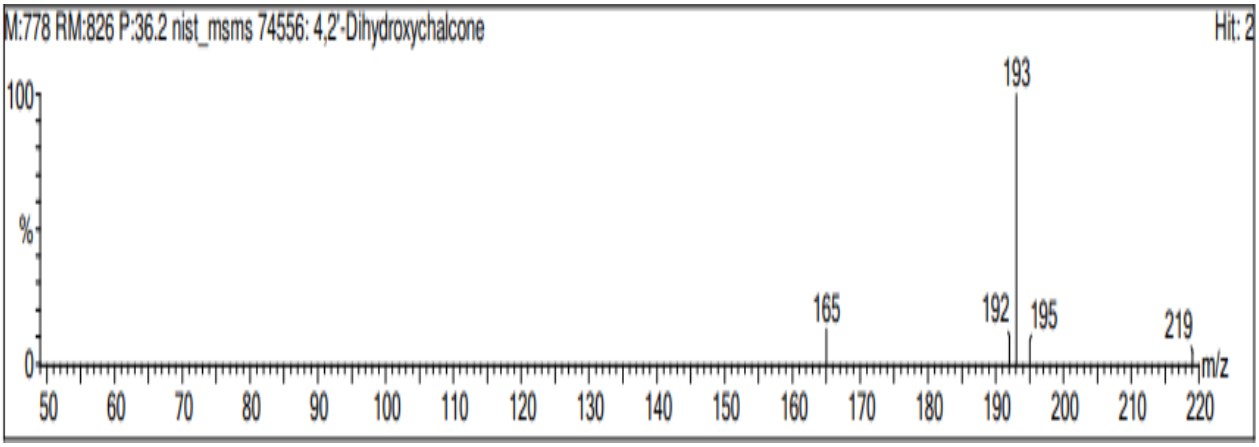


Figure 2



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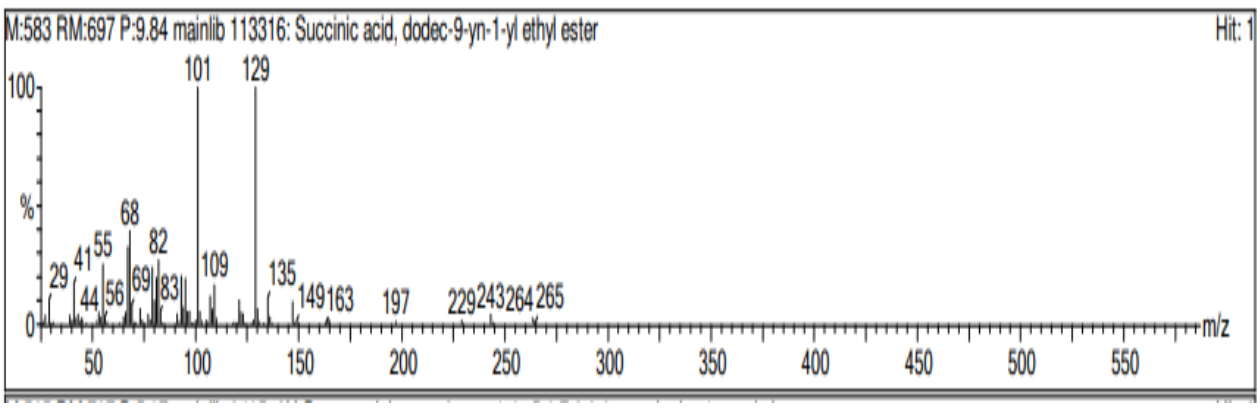

Figure 4

Figure 1- 4. GCMS results of Bioactive Compound Amoxapine, 4,2'-Dihydroxychalcone, Succinic Acid

Synephrine promotes the glucose consumption in skeletal muscles by activating AMPK pathway and suppresses the formation of glucose in liver cells and those effects elucidate peripheral utilisation of glucose, mitigates the active mechanism of glucose release into blood leading to maintenance of normal blood glucose level. It acts as an antiobesity agent by reducing the increased cholesterol and triglycerides levels [28, 29]. One of post-operative complications of cardiac surgery, arrhythmias that affects the rhythmicity of heart with detritions of cardiac muscle can also be treated with sotalol [30].

Dyphylline acts as a bronchodilator in respiratory disorder patients. It suppresses the allergic reaction induced by antigens with less side effects compared with theophylline. Thus, this drug is a good treatment for respiratory diseases [31]. Reports reveal that it possesses positive ionotrophic effect in the myocytes following sufficient vasodilation without increase in heart rate and thereby maintains good cardiac index [32].

Benzene, 3-[3-iodo-2-(iodomethyl)-2-methylpropyl]-1,2,4,5-tetramethyl possesses cytotoxicity effects and acts as an antitumor and anticancer activites [33].

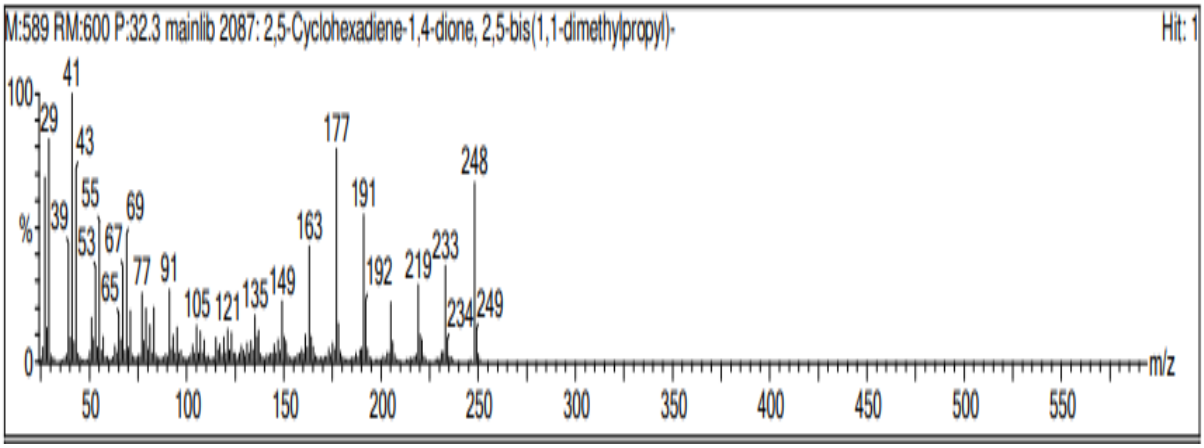

Figure 5

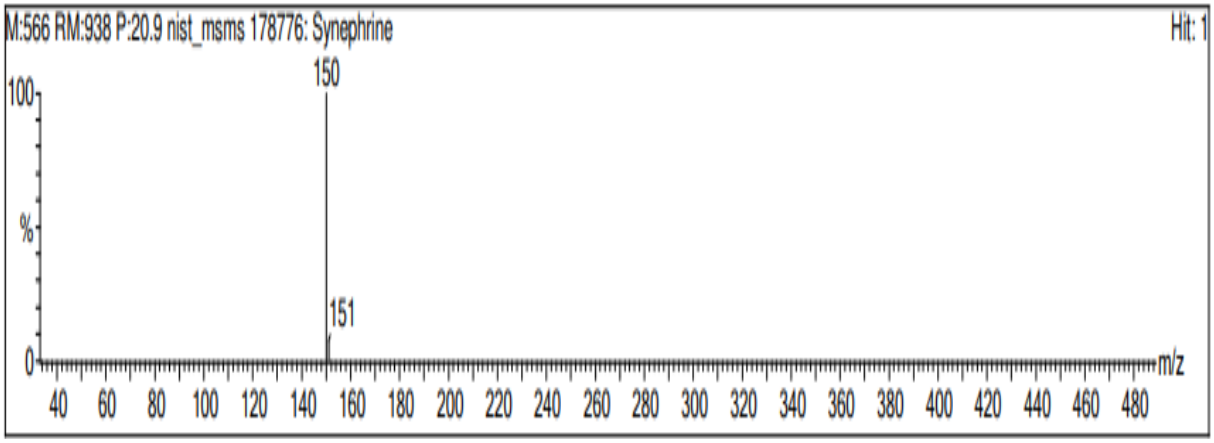

Figure 6

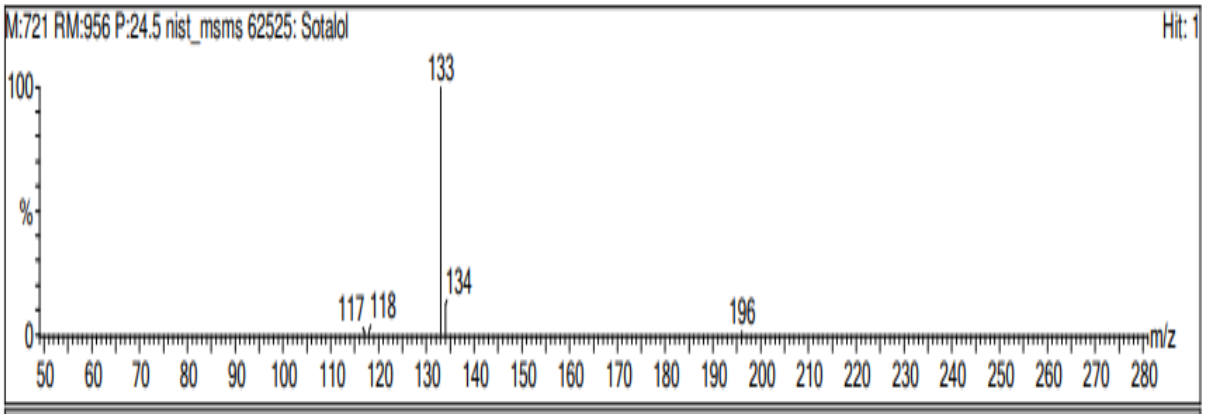

Figure 7

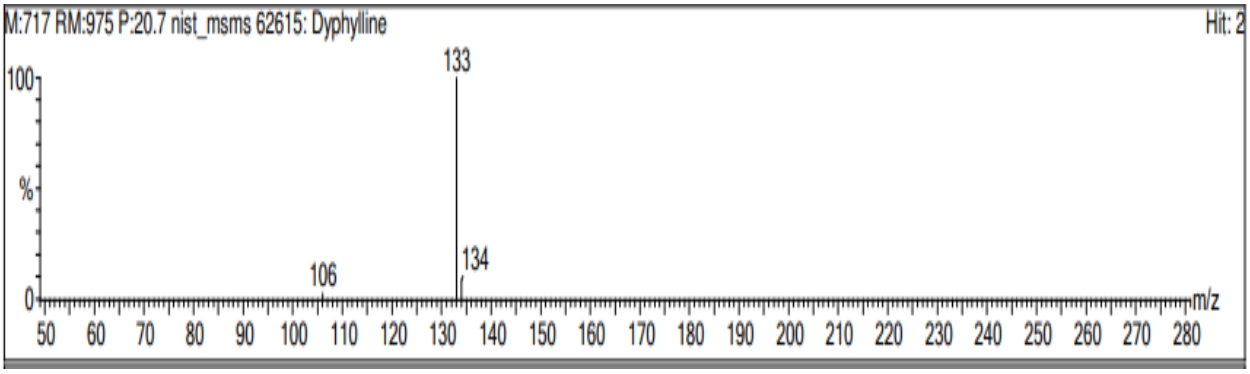

Figure 8

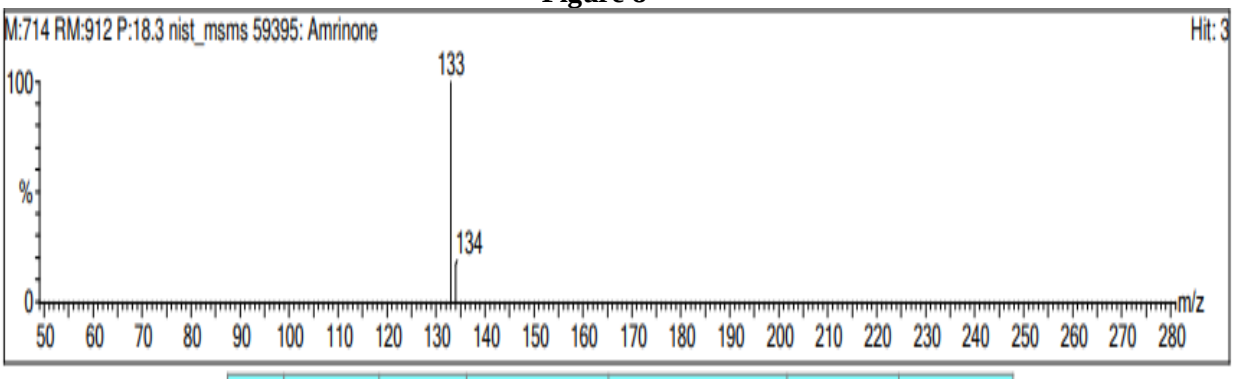

Figure 9

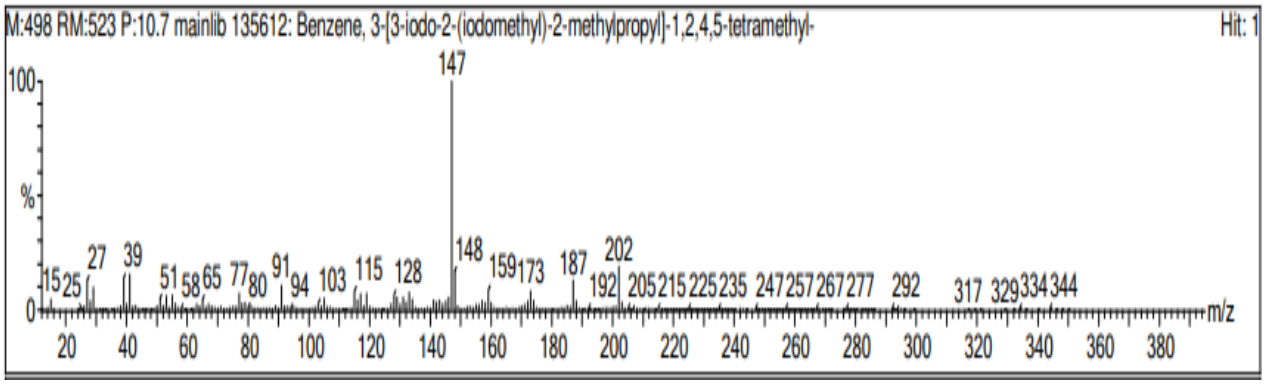

Figure 10

Figure 5-10. GCMS results of bioactive compound 2,5-Cyclohexadiene-1,4-dione, 2,5-bis(1,1-dimethylpropyl)-, Synephrine, Sotalol, Dyphylline, Amrinone, Benzene, 3-[3-iodo-2-(iodomethyl)-2-methylpropyl]-1,2,4,5-tetramethyl—

Conclusion

Thus, the present study revealed the phytochemical and bioactive compounds, alkaloids, sterols, glycosides, saponins, carbohydrates, flavonoids, tannins and proteins possesses immense medicinal values and also assists the physiological activities of Trikatu. Thus, the compounds of Trikatu formulation possesses good medicinal properties with substantial evidence, it can be incorporated in the manufacture of commercial drugs as an effective herbal formulation.

Acknowledgement

I am grateful to my Guide, Co-Guide, and my Mentors for helpful comments during the preparation of this manuscript. Authors would like to thank Shri Sathya Sai Medical college & research institute, for the necessary facilities provided.

Conflict of Interest

There exist no conflicts of interest, as stated by the authors.

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