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ANTIBACTERIAL, ANTIOXIDANT ACTIVITY AND GC MS ANALYSIS OF A SIDHA MEDICINE “NEERKOVAI TABLETS”.

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Abstract

Neerkovai is a sidha medicine for the treatment of Sinusitis. Nine plant components and borax dehydrate are the constituents of this medicine. The present work embarks upon the antibacterial, antioxidant and GC MS analysis of this medicine. It was found that Neerkovai works as a mild antibacterial against pathogens like *Staphylococcus aureus*, *Streptococcus pyogenes*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* at higher doses of 12.5, 25, 37.5 and 50 mg/ml of distilled water solutions.

The antioxidant study revealed that in all the three assays, namely DPPH, FRAP and Hydrogen peroxide scavenging, Neerkovai gave highest activity in Ethanol solution as compared to methanol and water solutions. The GC MS analysis indicated the presence of important medicinal bio molecules, such as Isoborneol, Eugenol, Ar-tumerone, Desmethylnomifensine, Piperine, Isoquinoline, 1,2,3,4-tetrahydro-8-amino-2-methyl-4-phenyl, Dehydroabietic acid, Abietic acid, β -Pimaric acid, Oleic Acid, n -Hexadecanoic acid, Ar-tumerone, Phenol, 2,4-bis(1,1-dimethylethyl)-, Geranyl-p-cymene. The biological activity of some of the compounds which were present in high quantities such as, Phenol, 2-methoxy-4-(2-propenyl)-, acetate, Benzenepropanoic acid, β,β -dimethyl-, methyl ester, 6-(p-Tolyl)-2-methyl-2-heptenol, trans-, Curlone, Phenol, 2-methyl-5-(1,2,2-trimethylcyclopentyl)-, (S)- is hitherto not known and further work

is in progress to understand the mechanism of these compounds as well as that of Neerkovai to establish its medicinal efficacy.

Key Words: Neerkovai, Antioxidant, Antibacterial, GC MS, Piperine, Eugenol, Isoborneol.

Introduction

The role of sidha and Ayurvedic medicines is immense due to their increasing acceptance by traditional and modern medical practitioners. This change in trend is due to the surge in complementary and alternative medicine research for obvious reasons of cost effectiveness, less side effects and easy availability. The lack of scientific approach towards identifying the medicinal efficacy of such systems, like dose specificity, contraindications, short and long term effects, lack of enough feedback statistics, lacunae in procurement, preparation, packing, storage and transport of such medicines etc. makes such systems universally unacceptable. Compared to the literature available in modern medical practice the scientific data on all the above parameters in Sidha and Ayurvedic medicinal practice is very scarce. The World health Organization also has recognized the importance of traditional medicines and has been active in creating strategies, guidelines and standards for botanical medicines ^[1]. More focus and attention is warranted from all the stakeholders like medical practitioners, researchers, Government organizations, NGOs, rural, folk and tribal participants etc. in this regard to bring these age old systems of medicine to the fore towards a safe and healthy mankind. Some of the reports on the medicinal aspects of Sidha and Ayurvedic medicines are available. ⁽²⁻²⁰⁾ Present study is an attempt to understand the antibacterial, antioxidant and GC MS analysis of one Sidha drug, Neerkovai tablets.

Neerkovai Mathirai (Tablet) is a Sidha medicine used to cure Sinusitis or Peenism. This disease is characterized by reddening of nasal mucosa, rhinitis, headache, and intermittent expulsion of mucous, purulent or bloody sputum. The patient complaints such as burning sensation, itching with reddening coupled with watering of nasal mucosa and eyes, irritation of ears with obstruction, severe headache with dyspnoea and rhinitis. The reason for this disease could be intake of cold water, exposure to cold climate, inhalation of smoke or other polluting gases, sleeplessness, talking in high pitched voice etc.

The textual reference for this medicine is *Siddha Vaidya thirattu*’.

This medicine has the following ingredients:

1. Turmeric: (*Curcuma longa*): 40 grams

2. Kasturi Turmeric: (*Curcuma aromaticus*): 40 grams
3. Borax dehydrates: 20 grams
4. Benzoin Resin: (*Styrax tonkinensis*): 20 Grams
5. Pepper: (*Piper nigrum*): 20 grams
6. Dried Ginger: (*Zingiber officinale*): 20 grams
7. Nutmeg: (*Myristica fragrans*): 20 grams
8. Ajwain: (*Carom*) (*Trachyspermum copticum*): 10 grams
9. Clove: (*Syzygium aromaticum*): 10 grams
10. Camphore: (*Cinnamomum reticulate*): 10 grams
11. Lime juice: (*Citrus reticulate*): Sufficient Quantity

The above ingredients are powdered thoroughly and mixed in lime juice to make a paste. The paste is either sun dried or made into tablets in machine. The tablets are rubbed in little quantity of water and applied over the fore head to relieve sinusitis, persistent headaches due to cold etc. This medicine is manufactured by a number of Pharmaceutical companies in India.

The use of the specified ingredients for the preparation of Neerkovai tablets indicate that all the above constituents must have similar medicinal properties or contribute to the purpose of this medicine. The medicinal properties of the constituents are mentioned below:

Turmeric - (*Curcuma longa*)

Turmeric has wide applications in food, medicine preservation. Turmeric is anti-inflammatory, antimicrobial, preservative, antifungal, anticancer, cardio protective, hyperglycemic and anti-diabetic. ^[21-25]

Wild turmeric (*Curcuma aromaticus*)

Sikha et al, 2015 have reviewed the various medicinal properties of wild turmeric. ^[26] Wild turmeric has activities like anti-inflammatory and wound healing (Kumar et al, 2009), promotes apoptosis, as antioxidant, renal protective against arsenic poisoning, as antitussive and as inhibitory to platelet aggregation. ^[27-32] This rhizome is also a potential medicine having antibacterial, anti-inflammatory and anticancer, skin care, antioxidant and antitumor. ^[33]

Dehydrated borax – Poritha vengaram

Borax is an antidote for fluoride toxicity and removes fluorides from body.^[34] It is a good internal and external fungicide, reduce serum triglyceride levels, stabilizes hormone production, works as anti-inflammatory and aphrodisiac, helps heal wounds, removes toxins as chelator, stabilizes calcium, copper and magnesium levels in blood and helps in improving metal faculties.^[35-38]

Gum benzoin – Sambrani (*Styrax tonkinensis*)

Benzoin is used for the treatment of hyper bilirubinemia by rural people of Andhra Pradesh, India due to lack of modern medical facilities there. Raju *et al*, 2011 have shown its effect of serum bilirubin levels on jaundice induced rats.^[39] It possesses antiseptic, carminative, expectorant and diuretic properties.

Black pepper – kuru milaku (*Piper nigrum*)

Black pepper is a common spice. This is a dried unripe fruit of the climbing plant belonging to family Piperaceae. The dried or fried seeds are powdered used for various culinary and medicinal purposes. In Ayurveda it is known as Kapha virodhini (works against Phlegm). The decoction of Pepper is used for curing cough. This is also digestive stimulant and used for treatment of diarrhea, lack of appetite and dyspepsia.^[40]

Sunthi - Dry ginger – Chukku (*Zingiber officinale*)

Ginger is one of the household medicines used against common cold, cough and indigestion. Its medicinal values are well documented.^[41] Adel and Prakash, 2014 have reported its antioxidant properties.^[42] Ginger controls vomiting and nausea during pregnancy and also controls blood pressure by blocking calcium channels.^[43, 44]

Nutmeg – Jathikkai (*Myristica fragrans* Houtt.) is yet another spice used widely in Indian culinary practice for its characteristic fragrance. It has medicinal properties such as, antibacterial, antiviral, anti diabetic, anti leukemic etc.^[45]

Iyer *et al*, 2009, have reported the medicinal potential of nutmeg.^[46]

Ajwain – Omum (*Trachyspermum copticum*)

Carom seeds are traditionally used as a home remedy for flatulence and indigestion. Boskabady *et al*, 2014, have elaborated the medicinal values of this seed.^[47] It has a range of medicinal values such as, carminative, antiseptic, expectorant, anti-parasitic, anti plate aggregator and as anti lithiasis.^[48] It is also known as diuretic, anti carcinogenic and is a potential foetotoxic.^[49-51]

Cloves – Lavangam (*Syzygium aromaticum*)

Cloves are rich source of phenolic compounds like eugenol and gallic acid, which have medicinal properties such as antioxidant, antimicrobial, antiviral and also cytotoxic. [52-55]

Camphor – Karpooram (*Cinnamomum reticulata*)

Camphor also has a number of medicinal values such as topical analgesic, antiseptic, antispasmodic, anti inflammatory, expectorant and as cold suppressant. [56, 57] It is used for asthma, bronchitis and rheumatism. [58]

Lime (*Citrus aurantifolia*)

Sweet lime or lime is a common citrus fruit used widely all over the world. It is rich in flavonoids, citric acid and terpens. All these three compounds have great medicinal values, particularly as antioxidants and as vitamins. The oil from the peels also has strong medicinal properties. [59, 60]

The present work encompasses the antimicrobial, antioxidant and GC MS analysis study of Neerkovai tablets. The antibacterial study gives a clear understanding of this medicine against sinusitis, bronchitis and other lung infections. The antioxidant study would indicate its role as a medicine in curing the lung related diseases. The GC MS analysis would give a picture of the similarities the bio molecules with those present in individual plant components or may reflect the medicinal role of each plant as mentioned earlier. It is also possible that some new compounds could be formed during the processing of the medicine which might show in the GC MS analysis and it is quite possible that these new compounds could have better medicinal properties as compared to those of the constituents. The GC MS results could prove the efficacy of this medicine thus giving an insight about the choice of the ingredients; their proportions etc. indicating the scientific knowledge the sidha proponents had in formulating this medicine.

Materials and Methods

The Sidha medicine was procured from standard Sidha medical shop at Chennai.

A. Antimicrobial study

The microbes on which the antimicrobial activity was performed were *Staphylococcus aureus*, *Streptococcus pyogenes*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*. The antibacterial study was undertaken using water solution of Neerkovai at different concentrations of the samples (40, 60 and 80µg/ml) using hot percolation method and it was found that there was no action. At higher concentrations (12.5, 25, 37.5, 50 mg/ml) of Neerkovai there was minimal antibacterial activity.

B. Antioxidant Study

Antioxidant study was performed by DPPH Assay, FRAP Assay and Hydrogen Peroxide Scavenging Activity assay.

DPPH Assay (1,1-diphenyl-2-picrylhydrazyl) (Bliss, 1958)^[61]

The sample was dissolved in 3 different solvents (Ethanol, Methanol and Water) in 1mg/ml concentration and used as stock. From the stock, various concentrations (100, 200, 300, 400mg) were taken for further analysis.

Respective solvents were taken as negative control.

Conc. = Concentration of the sample

OD = OD of the sample

Neg. Control = The Solvent

Activity = $\text{Neg. Control} - \text{OD} / \text{Neg. Control}$

% of Activity = $\text{Activity} / 100$

IC50 = $50 - c \text{ value} / m \text{ value}$

IC50/ml = $\text{IC50} / 3$ (3 ml of DPPH for the assay. To find the activity in 1 ml, the value had been divided by 3).

FRAP Assay (Ferric Reducing/Oxidant Power) (Pulido et al., 2000)^[62]

Neerkoai was dissolved in Ethanol, Methanol and Water. Triplicates had been put for all the Processes.

Conc. = Concentration of the sample

OD = OD of the sample

Linearity (y) = $mx + c$

M = Slope

C = The point x crosses y axis

X = $\text{OD} - c \text{ value} / m \text{ value}$

mM Fe/mg = $X \text{ value} / \text{concentration} \times 1000$

Mean = Average of mM Fe/mg

STDEV = Standard Deviation for mM Fe/mg.

Hydrogen Peroxide Scavenging Activity (Ruch et al. 1989)^[63]

Neerkovai was dissolved in Ethanol, Methanol and Water.

Triplicates had been put for all the Processes.

Conc. = Concentration of the sample

OD = OD of the sample

Neg. control = The solvent

Activity = Negative control – OD / Negative control

% of activity = Activity / 100

Mean = Average of % of Activity

STDEV = Standard Deviation of % of Activity

Graph = (For Mean of % of Inhibition vs samples) Drawn using 2D clustered column.

C. GC MS Analysis of Neerkovai.

The medicine, Neerkovai was subjected to GC MS analysis as per standard procedure. The metabolites in the samples were identified using a P2010 gas chromatography with thermal desorption system TD20 coupled with mass spectroscopy (Shimadzu). The ionization voltage 70ev and GC was conducted in the temperature programming mode with a Restek column (0.25mm, 60m, XTI-5). The temperature in the initial column was 80⁰c for 1 min, and then increased linearly to 70⁰c to 220⁰c held for 3 min followed by linear increased temperature 100⁰ c up to 290⁰c and held for 10min.

The injection port temperature was 290⁰ c and the GC/MS interface was maintained at 29⁰c, the samples were introduced via an all glass injector working in the split mode with helium carrier gas low rate with 1.2 ml per minute. The identification of metabolites was accomplished by comparison of retention time and fragmentation pattern with mass spectra in the NIST spectral library stored in the computer software (version 1.10 beta, Shimadzu) of the GC-MS. The relative percentage of each extract constituent was expressed with peak area normalization.

Results and Discussion

A. Antibacterial study results

The antimicrobial activity of Neerkovai against the selected pathogens has indicated minimal activity as seen by zones of inhibition when compared to standard drugs. The results indicated that Neerkovai have very less antimicrobial activity.

(Figure 1).





Microbe	Sample – Neerkovai
<i>Staphylococcus aureus</i>	
<i>Streptococcus pyogenes</i>	
<i>Pseudomonas aeruginosa</i>	
<i>Klebsiella pneumoniae</i>	

Figure-1: Indicating the antimicrobial activities of Neerkovai on selected pathogens.

B Antioxidant Study Results

B1. DPPH Assay

Table No.1 indicates the antioxidant activity of Neerkovai by DPPH assay.

From the Table No.1 the lowest IC50/ml value (320.3551) was found in Ethanol extract which gave the highest activity (106.785) as compared to methanol and water extracts of Neerkovai.

Thus it was found that among the three extracts of Neerkovai, the best antioxidant activity was observed in Ethanol extract whereas the activities were less in methanol and water extracts.

B2. FRAP Assay

Table No 2 indicates the antioxidant activity of Neerkovai by FRAP assay.

It was observed that in the ethanol extract the mM Fe/mg of sample showing 204.77 was the highest when compared to methanol and water sample values of 201.24 and 117.30, respectively.

B3. Hydrogen Peroxide Scavenging Activity

Table No 3 indicates the hydrogen scavenging activity of Neerkovai.

It was found that Neerkovai indicated maximum activity in ethanol solution when compared with methanol and water (4.92, 4.60 and 3.90 respectively)

B1. DPPH Assay

Table No.1 indicates the antioxidant activity of Neerkovai by DPPH assay.

DPPH ASSAY

	Conc	OD	negative control	Activity	% of activity	m value	c value	IC 50	IC 50/ml
	0				0				
Ethanol	100	0.886	1.295	0.31583	31.58301158	0.138	5.791	320.3551	106.785
	200	0.875	1.295	0.324324	32.43243243				
	300	0.822	1.295	0.365251	36.52509653				
	400	0.432	1.295	0.666409	66.64092664				
Methanol	100	1.144	1.295	0.116602	11.66023166	0.098	3.135	478.2143	159.4048
	200	0.892	1.295	0.311197	31.11969112				
	300	0.871	1.295	0.327413	32.74131274				
	400	0.793	1.295	0.387645	38.76447876				
Water	100	1.263	1.295	0.02471	2.471042471	0.108	4.957	508.8611	169.6204
	200	1.178	1.295	0.090347	9.034749035				
	300	0.861	1.295	0.335135	33.51351351				
	400	0.793	1.295	0.387645	38.76447876				

B2. FRAP Assay

Table No 2 indicates the antioxidant activity of Neerkovai by FRAP assay.

Sample	CONC (µg)	OD	m value	c value	X	mM Fe (II)/mg	Mean (mg)	STDEV
Ethanol	100	0.686	0.0274	0.1086	21.07299	210.729927		

	100	0.688	0.0274	0.1086	21.14599	211.459854		
	100	0.635	0.0274	0.1086	19.21168	192.1167883	204.77	10.96
Methanol	100	0.641	0.0274	0.1086	19.43066	194.3065693		
	100	0.648	0.0274	0.1086	19.68613	196.8613139		
	100	0.691	0.0274	0.1086	21.25547	212.5547445	201.24	9.88
Water	100	0.447	0.0274	0.1086	12.35036	123.5036496		
	100	0.418	0.0274	0.1086	11.29197	112.919708		
	100	0.425	0.0274	0.1086	11.54745	115.4744526	117.30	5.52

B3. Hydrogen Peroxide Scavenging Activity

Table No 3 indicates the hydrogen scavenging activity of Neerkovai.

Solvent	Conc.	OD		Neg. Control	% Activity	Mean	STDEV
Ethanol	100	0.457	0.748	0.389037	38.90374332		
	100	0.384	0.748	0.486631	48.6631016		
	100	0.412	0.748	0.449198	44.9197861	44.16	4.92
Methanol	100	0.548	0.748	0.26738	26.73796791		
	100	0.614	0.748	0.179144	17.9144385		
	100	0.598	0.748	0.200535	20.05347594	21.57	4.60
Water	100	0.648	0.748	0.13369	13.36898396		
	100	0.649	0.748	0.132353	13.23529412		
	100	0.699	0.748	0.065508	6.550802139	11.05	3.90

Results of GC MS Analysis of Neerkovai

Figure-2. GC MS graph of Neerkovai. Table 4. Indicating retention time, Molecular structure, Molecular weight and % peak values of various bio molecules found in GC MS analysis.

From the GC MS analysis a number of compounds were identified of which the following were present in high quantities and a few were in minute quantities. Among the major molecules the important ones which show biological and medicinal activities are described.

Results of GC MS Analysis of Neerkovai

File :D:\MassHunter\GCMS\1\data\Karthik\A1.D
 Operator :
 Acquired : 09 Jul 2015 12:38 using AcqMethod Karthik.M
 Instrument : GC-MS
 Sample Name : A1
 Misc Info :
 Vial Number : 4

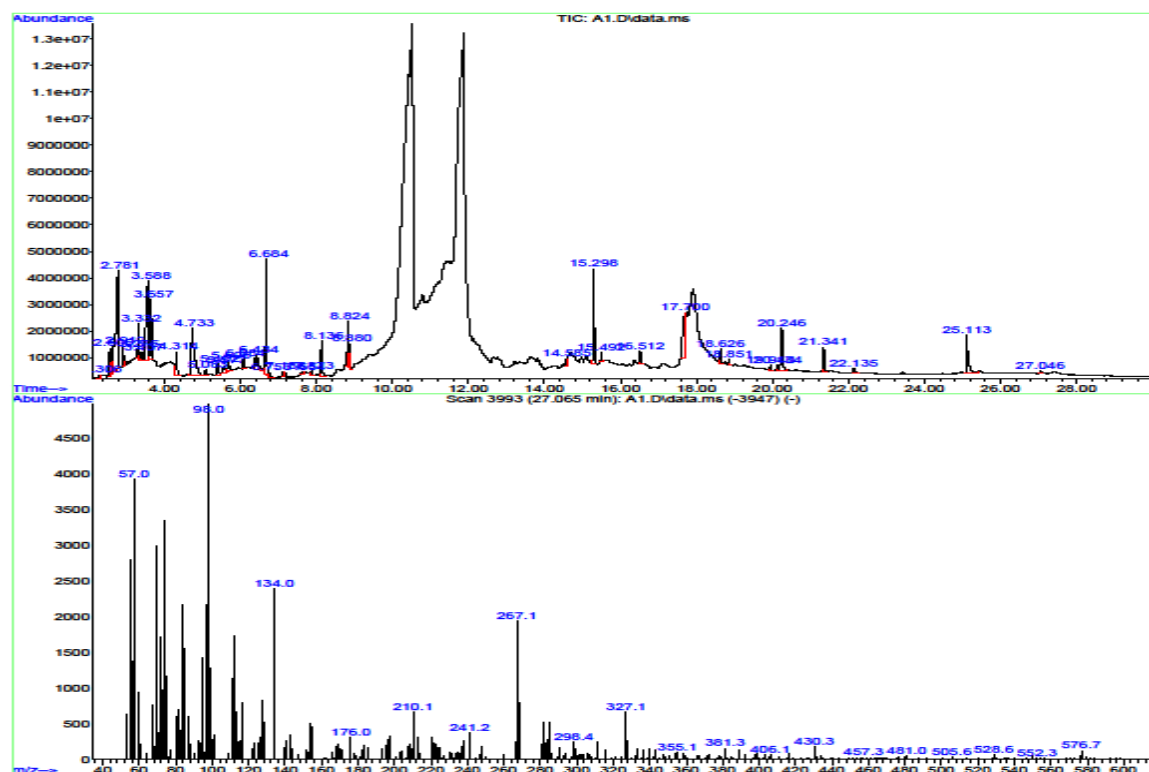


Figure-2: GC MS graph of Neerkovai.

Table-4: Indicating retention time, Molecular structure, Molecular weight and % peak values of various bio molecules found in GC MS analysis.

Sl No	Retention Time (Min)	Name of Compound	Mol. Structure	Mol. Weight	Peak (%)
1.	9.900	Iso-borneol	C ₁₀ H ₁₈ O	154	4.551
2.	10.588	Endo-Borneol	C ₁₀ H ₁₈ O	154	0.218
3.	12.246	Thymol	C ₁₀ H ₁₄ O	150	1.241
4.	13.265	Eugenol	C ₁₀ H ₁₂ O ₂	164	1.495
5.	14.948	geranyl-p-cymene	C ₂₀ H ₃₀	270	1.018
6.	15,248	Tridecane, 2-methyl-2-phenyl-	C ₂₀ H ₃₄	274	0.128
7.	15.292	Phenol, 2,4-bis(1,1-dimethylethyl)-	C ₁₄ H ₂₂ O	206	1.389
8	15.492	Phenol, 2-methoxy-4-(2-propenyl)-, acetate	C ₁₂ H ₁₄ O ₃	206	1.615

9.	15.842	Asarone	C ₁₂ H ₁₆ O ₃	208	0.403
10.	16.180	Benzenepropanoic acid, β,β -dimethyl-, methyl ester	C ₁₂ H ₁₆ O ₂	192	2.453
11.	16.324	Caryophyllene oxide	C ₁₅ H ₂₄ O	220	0.411
12.	16.524	geranyl- α -terpinene	C ₂₀ H ₃₂	272	0.404
13.	16.637	Calarene epoxide	C ₁₅ H ₂₄ O	220	0.132
14.	16.756	α -acorenil	C ₁₅ H ₂₆ O	222	0.155
15.	16.837	(-)-Spathulenol	C ₁₅ H ₂₄ O	220	0.283
16.	16.881	Benzenebutanal, $\gamma,4$ -dimethyl-	C ₁₂ H ₁₆ O	176	0.305
17.	16.950	Tetracyclo[6.3.2.0(2,5).0(1,8)]tridecan-9-ol, 4,4-dimethyl-	C ₁₅ H ₂₄ O	220	0.156
18.	17.037	γ -Himachalene	C ₁₅ H ₂₄	204	0.143
19.	17.131	6-(p-Tolyl)-2-methyl-2-heptenol, trans-	C ₁₅ H ₂₂ O	218	2.711
20.	17.200	Ar-tumerone	C ₁₅ H ₂₀ O	216	6.899
21.	17.331	2,5-Octadecadiynoic acid, methyl ester	C ₁₉ H ₃₀ O ₂	290	0.338
22.	17.631	Curlone	C ₁₅ H ₂₂ O	218	2.120
23.	17.769	Longiverbenone	C ₁₅ H ₂₂ O	218	0.209
24.	18.151	Phenol, 2-methyl-5-(1,2,2-trimethylcyclopentyl)-, (S)-	C ₁₅ H ₂₂ O	218	8.672
25.	18.445	Thymol	C ₁₀ H ₁₄ O	150	2.928
26.	18.851	i-Propyl 12-methyl-tridecanoate	C ₁₇ H ₃₄ O ₂	270	0.182
27.	18.689	Isoborneol, heptafluorobutyrate (ester)	C ₁₄ H ₁₇ F ₇ O ₂	350	0.382
28.	18.914	Arteannuic acid	C ₁₅ H ₂₂ O ₂	234	0.143
29.	19.158	2-(4a,8-Dimethyl-6-oxo-1,2,3,4,4a,5,6,8a-octahydro-naphthalen-2-yl)-propionaldehyde	C ₁₅ H ₂₂ O ₂	234	0.428
30.	19.621	Acetic acid, 2-methylene-bicyclo[3.2.1]oct-6-en-8-yl ester	C ₁₁ H ₁₄ O ₂	178	0.602

31.	19.827	Pentadeca-2,3,6,9,12,13-hexaen-8-one, 2,5,5,11,11,14-hexamethyl-	C21H30O	298	0.185
32.	19.890	Valtrate	C22H30O8	422	0.633
33.	19.940	7,9-Di-tert-butyl-1-oxaspiro(4,5)deca-6,9-diene-2,8-dione	C17H24O3	276	0.301
34.	20.115	1-Hexen, 2-(p-anisyl)-5-methyl-	C14H20O	204	5.169
35.	20.252	n-Hexadecanoic acid	C16H32O2	256	2.248
36.	20.609	2(1H)-Naphthalenone, 4a,5,6,7,8,8a-hexahydro-6-[1-(hydroxymethyl)ethenyl]-4,8a-dimethyl-, [4ar-(4a α ,6 α ,8a β)]-	C15H22O2	234	0.243
37.	21.960	Oleic Acid	C18H34O2	282	1.919
38.	22.148	Androst-5-en-3-ol, 4,4-dimethyl-, (3 β)-	C21H34O	302	0.843
39.	22.961	Podocarp-7-en-3-one, 13 β -methyl-13-vinyl-	C20H30O	286	0.393
40.	23.705	Podocarp-7-en-3 β -ol, 13 β -methyl-13-vinyl-	C20H32O	288	0.205
41.	23.562	1-Phenanthrenecarboxylic acid, 7-ethenyl-1,2,3,4,4a,4b,5,6,7,8,10,10a-dodecahydro-1,4a,7-trimethyl-, methyl ester, [1R-(1 α ,4a β ,4b α ,7 α ,10 α)]-	C21H32O2	316	0.157
42.	23.899	Methyl dehydroabietate	C21H30O2	314	0.876
43.	24.049	β -Pimaric acid Abietic acid	C20H30O2	302	5.811
44.	24.412	Abietic acid	C20H30O2	302	9.415
45.	24.725	Dehydroabietic acid	C20H28O2	300	5.921
46.	25.088	Abietic acid	C20H30O2	302	6.428
47.	28.660	Isoquinoline, 1,2,3,4-tetrahydro-8-amino-2-methyl-4-phenyl-	C16H18N2	238	1.140
48.	29.717	Piperine	C17H19NO3	285	11.589
49.	30.618	Desmethylnomifensine	C15H16N2	224	2.578

1. Iso-borneol: Isoborneol is reported to have antiviral properties on herpes simplex virus 1 (HSV-1).^[64]
2. Thymol: Thymol is reported to have hair growth potential.^[65] Thymol derivatives have antioxidant, antibacterial and anti-inflammatory activities.^[66, 67, 68]
3. Eugenol: Synthetic Eugenol has been reported to have many important medicinal properties as is described by many reporters. It is an antifungal agent particularly against *Candida albicans*.^[69] Eugenol is a powerful fat soluble antioxidant and maintains the activities of the body antioxidant enzymes.^[70] Pharmacologically eugenol has been reported as anticonvulsant and local anaesthetic, antistress and bacteriostatic and bactericidal.^[71] Rompelberg *et al*, 1996, have demonstrated the effect of eugenol on the genotoxicity of established mutagens in liver.^[72] Anticarcinogenic potential of Eugenol was reported by Zheng *et al*, 1992.^[73] It depresses activity of central nervous and neuromuscular function.^[74] It also prevents radiation induced chemical oxidative damage in cell membranes and modifies the membrane associated signaling process after radiation exposure.^[75] It possesses antiviral activity *in vitro* and *in vivo* against human herpes virus^[76]. Eugenol was found to induce apoptosis in melanoma cells and HL-60 leukemia cells.^[77, 78] Moreover, it has been reported that dimers of eugenol related compounds have a better antioxidant activity than the original monomers^[79]. Eugenol is hepatotoxic and overdose cause convulsions, diarrhea, nausea, unconsciousness, dizziness, rapid heartbeat and it also cause allergic reactions.
4. Geranyl-p-cymene- P-Cymene is an antioxidant and as antinociceptive^[80, 81]
5. Phenol, 2, 4-bis(1,1-dimethylethyl)- : Phenol, 2, 4-bis (1, 1-dimethylethyl) – derivative is known for its antibacterial, antioxidant and anti-inflammatory activities.^[82, 83, 84]
6. Ar-tumerone: Tumerone acts as antivenom, anticancer and as antioxidant^[85]
7. n -Hexadecanoic acid: n- Hexadecanoic acid is reported to have activities like antioxidant, hypocholesterolemic, nematocide, anti androgenic, as flavoring agents, hemolytic, antibacterial, cytotoxic and as 5-alpha reductase inhibitor^[86, 87, 88].
8. Oleic Acid: Oleic acid is reported to be Antitumor^[89]
9. β -Pimaric acid: β -Pimaric acid is a matrix metalloproteinase (MMP)-9 inhibitor^[90].
10. Abietic acid: Abietic Acid is a potent testosterone 5 α -reductase inhibitor, a cancer inhibitor, antioxidant, antibacterial and antiacetylcholinesterase^[91, 92, 93]

11. Dehydroabiatic acid: This is reported to be antiulcer, antimicrobial, anxiolytic, antiviral, antitumor and cytotoxic activities^[94]

12. Isoquinoline, 1, 2, 3, 4-tetrahydro-8-amino-2-methyl-4-phenyl-: This compound has biological activities such as anticancer, antimycobacterial, antimicrobial, anticonvulsant, anti inflammatory and cardiovascular.^[95]

13. Piperine: Piperine has diverse biological and supportive therapeutic activities like radioprotective, immunomodulatory and anti tumor activities, antidepressant, anticonvulsant, antinociceptive, and anti-arthritic^[96]. It helps in the absorption of selenium, vitamin B and Beta carotene as well as other nutrients. Among the various properties of piperine, the most important is that it facilitates the bioavailability of medicines by depressing the activity of drug metabolizing enzymes.^[97] Dendrite elongation inhibition activity was reported by Rao et al, 2012^[98].

14. Desmethylnomifensine: This compound is known for its antibacterial activity^[99]

To the best of our knowledge reports of medicinal values are not available for the following compounds which were present in high quantities such as Phenol, 2-methoxy-4-(2-propenyl)-, acetate, Benzenepropanoic acid, β,β -dimethyl-, methyl ester, 6-(p-Tolyl)-2-methyl-2-heptenol, trans-, Curlone, Phenol, 2-methyl-5-(1,2,2-trimethylcyclopentyl)-, (S)-. It will be of interest to know their medicinal values since they were present in substantial amounts.

Conclusions

It is concluded that the presence of Eugenol, Ar-tumerone, Isoborneol, Desmethylnomifensine, Piperine, Isoquinoline, 1,2,3,4-tetrahydro-8-amino-2-methyl-4-phenyl, Dehydroabiatic acid, Abietic acid, β -Pimaric acid, Oleic Acid, n - Hexadecanoic acid, Ar-tumerone, Phenol, 2,4-bis(1,1-dimethylethyl)-, geranyl-p-cymene etc. clearly indicate the antioxidant, antiviral and antibacterial potential of Neerkovai tablets as observed in our results. The present report is a part of work in progress to substantiate the exact medicinal efficacy of Neerkovai tablets for the cure of Sinusitis.

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