Research Article

Molecular modification for Synergism against Drug Resistant Bacteria: A Combinatorial Synthesis Approach using *Calitropis Procera* Extract with Ampicillin.

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ABSTRACT

Identifying novel methods to develop lead compounds for selectivity, efficacy, and safety for a clinical trial candidate remains a scientific challenge, Natural products offer novel pharmacophores, chemotypes, and scaffolds that can be amplified into efficient drugs for various infections and disease.

This study present a simple, basic and eco-friendly method for boosting the antimicrobial activity of two less effective antimicrobial agents to obtain repetitive constant synergism in combat drug resistant clinical bacteria. Aqueous extract of fresh *C. procera* leaves and flowers was made to react with 1 mg/mL ampicillin solution under heat and acidic condition. The prepared sample was synergistic and highly susceptible to resistant *S. aureus* and *Salmonella spp,* moving their zones of inhibition from 0 mm to 16.8 mm and from 5.3 mm to 21.4 mm respectively. Gas chromatography mass spectrometry, GC-MS analysis reveals the presence of 53 phytochemicals, oleic acid 13.04 %, 1,1,1,3,5,5,7,7,7-Nonamethyl-3-(trimethylsiloxy)tetrasiloxane 9.50 %, 9-Heptadecanone 3.75%, Cystamine 3.35 % and Tetrahydro-4H-pyran-4-ol 3.15 % were where the five (5) most abundant phytochemicals. Eighteen (18) out of the 53 phytochemicals were reported to have known biological activities thus, some undergo molecular transformation to a new molecule and/or analogue to existing biologically active compound due to the reaction condition used.

Farnesol, Cystamine, Cystine, Metaraminol, dl-phenylephrine and two different substitu**ted amphetamine** compounds were discovered**.** Three (3) phytochemicals present were reported to exhibit anticancer properties (**Farnesol, 4-amino-1-pentanol** and the of **imidazole** derivative similar to the drug **Ribavir**).

The results of this study reveals that medicinal plants phytochemicals can be used in synthetic combination reactions with themselves or other drug/reagent to produce vast array of compounds with good pharmacological activities or compounds which can be used as starting material, intermediates or derivatives in pharmaceutical production.

Keywords: *C.procera*, Ampicillin, Farnesol, Cystamine, Cystine, Metaraminol, dl-phenylephrine, Amphetamine.

1. INTRODUCTION

Ineffectiveness of antibiotics used for the treatment of infections and diseases due to bacteria resistance is of global concern [1]. With the increasing declines of new antibiotics, Identifying novel methods to develop lead compounds for selectivity, efficacy, and safety for a clinical trial candidate remains a scientific challenge, although, some synergistic drug combinations involving the use of two or more drugs that can work together to produce a more potent and targeted antimicrobial effect with different mechanisms of action to target multiple pathways simultaneously, is providing new ways in an effort to combat drug resistant in bacteria [2].

Minor changes in an antimicrobial agent chemical structure, such as geometry, stereochemistry, or functional group modifications, can impact its pharmacological activities [3].

The process of drug design, discovery, and development is a highly focused and challenging task for researchers. Synthetic reactions can be utilized to modify or create novel compounds derived from medicinal plants through structural modifications [4] semi-synthetic derivatives [5] prodrug synthesis [6] and combinatorial chemistry approach [7], leading to improved antimicrobial activities. Natural products offer novel pharmacophores, chemotypes, and scaffolds that can be amplified into efficient drugs for various infections and disease. They play a crucial role in drug design and development due to their chemical diversity and potential therapeutic properties [8-10]. They have been a prolific source of biologically active compounds, serving as the basis for numerous drugs.

Natural products have the inherent capacity to engage in various chemical reactions, leading to the formation of novel bioactive compounds, this ability arises from their diverse chemical structures and functional groups [11]. Natural products often contain functional groups that can undergo chemical transformations, such as oxidation, reduction, esterification, and alkylation, yielding derivatives with altered biological activities [12]. Semi-synthesis approach also can be employ in modifying a natural product using chemical reactions while retaining a portion of its original structure(s) [13]. Natural product libraries can be subjected to combinatorial chemistry techniques, allowing for the creation of diverse compound libraries with potential bioactivity [14].

Calotropis procera, commonly known as milkweed, its fresh juice of leaves and flowers were administered orally in the treatment of Malaria and intermittent fever, and in decoction for the treatment of Gonorrhoea [15].

Calotropis procera leaf aqueous chloroform AQC, aqueous methanol AQM, crude extract antibacterial screening showed an inhibition in *E.coli* of AQM 30 mm, AQC 20 mm and AQC 15 mm for *S. Aureus*. Screening of crude fractions of *Calotropis procera* (Linn) stem showed an inhibition of AQM 5 mm for *E.coli* and 21 mm *S.typhi* [16]. *C. procera* leaves extract was effective against *Staphylococcus aureus, Klebsiella pneumonia,* and *Escherichia coli*, with inhibition zones of 18.66 mm, 21.26 mm, and 21.93 mm, respectively. The plant extract was considered to be a moderate inhibitor against *Bacillus subtilis*, with MIC ranging from 0.60–1.50 mg/mL [17].

Gas chromatography-Mass spectrometry GC-MS analysis of methanol methanol stem, methanol aqueous stem, chloroform aqueous leaf, pet-ether acetone leaf, methanol methanol leaf, and methanol aqueous leaf extract of *C. Procera* shows the presences of various phytochemicals some of which include: Methyl palmitate, 9,12-Octadecadienoic acid (z,z)- methyl ester, 9-octadecadienoic acid, octadecadienoic acid, Methyl9,12-hepatadecadienoate, Tetradecanoic acid, (2,3-Diphenylcyclopropyl) methylphenyl sulfoxide, hexadecanoic acid, methyl ester, n-hexadecanoic acid, dodecanoic acid, linolenic acid, ethyl ester, among others. [15][16][17]18][19][20][21]22]

In this study, we aim to develop a method to achieve constant repetitive synergism between medicinal plant extract and ineffective antibiotics to combat drug resistance in clinical bacteria. Our objective is to employ the use of combinatorial chemistry techniques, carry out antimicrobial screening and GC-MS analysis for information of the transformation that occur within the mixture.

2. METHODS

2.1 Sampling

Ampicillin 500 mg 10 capsules produce by Sam-Ace Ltd. (Pharm. Man. Div) Plot 9/10 Block 7c Akoda Ind. Est. Osun State Nigeria was purchased from pharmaceutical vendors within the Kaduna metropolis, Kaduna North, Kaduna, Nigeria.

Calotropis procera plant leaves and flowers was collected in September 2023 at Sabon Tasha Kaduna and it was authenticated by a plant taxonomist in Ahmadu Bello University, Zaria Kaduna State, with the voucher number V/N-ABU900086.
Clinical Isolates of *Salmonella Spp* (Stool), and *Staphylococcus aureus* (High Vaginal Swab) were collected at Chemical Pathology, Hematology and Microbiology diagnostic laboratory of Oxford Hospital Makera, Kakuri, Kaduna State Nigeria.

2.2 Experimental

The method adopted by [1] was used. 10 g fresh leaves and flowers of *Calotropis procera* combined was washed with distilled water, taken into a blending machined, 100 mL of distilled water was added to it and was blend for homogeneity, it was then filtered using a what Mann no.1 filter paper to extract its juice. 1 mg/mL of Ampicillin solution was prepared. 2 mL of the prepared Amoxicillin solution was transferred into a test tube containing 2 mL of *C. procera* extract, 0.2 mL of concentrated tetraoxosulphate (vi) acid (H_2SO_4) was added to it (as shown in Figure 1), it was heated in a water bath at 110 °C for 10 minutes, it was then centrifuge and kept for further analysis.

2.3 Screening for antibiotic resistance and antimicrobial test of prepared samples

2.3.1 Materials required

- Mueller-Hinton agar (MHA)
- Antibiotic discs
- Cotton swabs
- Petri dishes
- 0.5 McFarland Turbidity standard
- Inoculum
- Forceps
- Metric rule

Salmonella spp (Stool) and *Staphylococcus aureus* (High Vaginal Swab) were isolated, characterized, and identified. The two bacteria isolates shown to be resistant to Amoxicillin, Septrin, Ampiclox, and Chloramphenicol in High profile positive/ negative 10 tipped multiple susceptibility antibiotic discs were then cultured for the prepared sample antimicrobial test. Kirby-Bauer disk diffusion test using Mueller-Hinton Agar (MHA) was used [1]. After 24 hours of incubation, a metric ruler was used to measure the Zone of Inhibition (ZOI), in millimetres according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI) [23].

2.4 Gas chromatography-mass spectrometry (GC-MS) analysis of prepared sample

For the determination of the phytochemicals contained in the prepared sample, Agilent 19091S-433UI Gas Chromatography-Mass Spectrometer (GC-MS) machine was used, HP-5ms Ultra Inert, 0 °C—325 °C (350 °C): 30 m x 250 µm x 0.25 µm. Pressure 7.3614 psi. Flow 0.97414 mL/min, Helium carrier gas, injector temperature program was 250°C and column temperature was 50^0C, Syringe Size 10 µL and Injection Volume 1 µL.

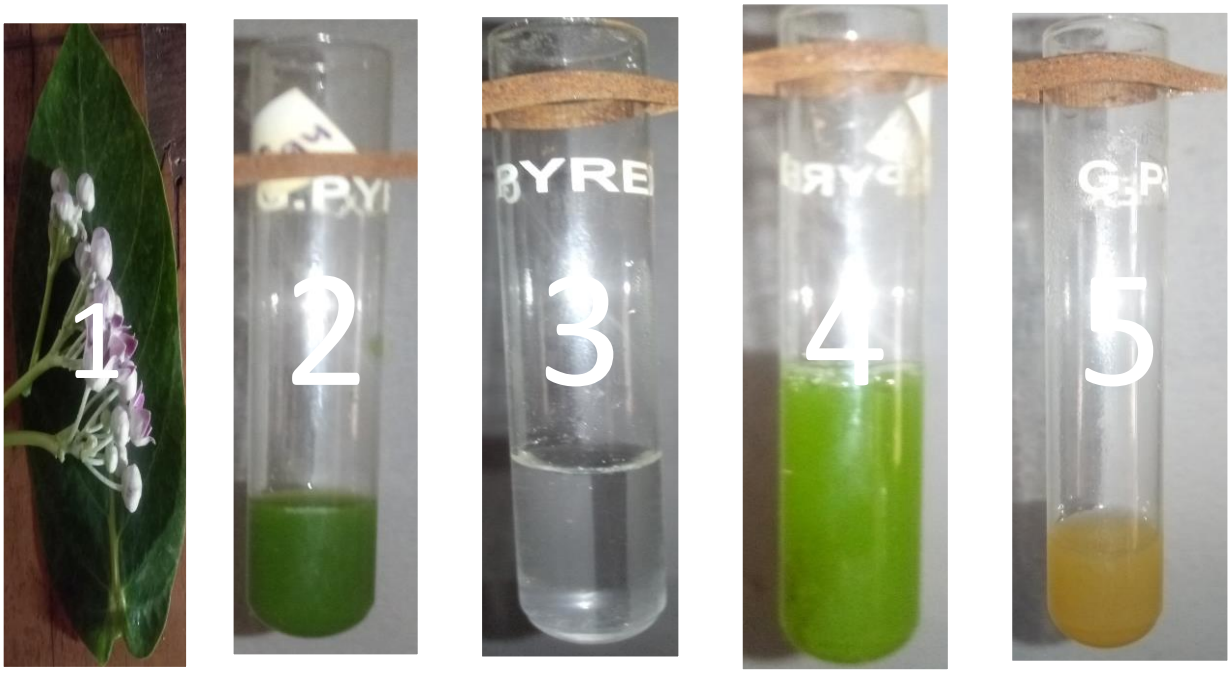

Figure 1. Sampling and stages in the preparation of the sample. 1: *C. procera* leaf and flowers, 2: *C. procera* extract, 3: Ampiclox solution, 4: Mixture before 5: Mixture after acid addition and heating.

3.0 Results and discussion

3.1 Gas Chromatography–Mass Spectrometry (GC–MS)

GC–MS analysis was carried out for the phytochemical study of the prepared sample labelled 5 in Figure 1. The chromatogram identified 53 phytochemicals as constituents (Table 1 and Figure 2).

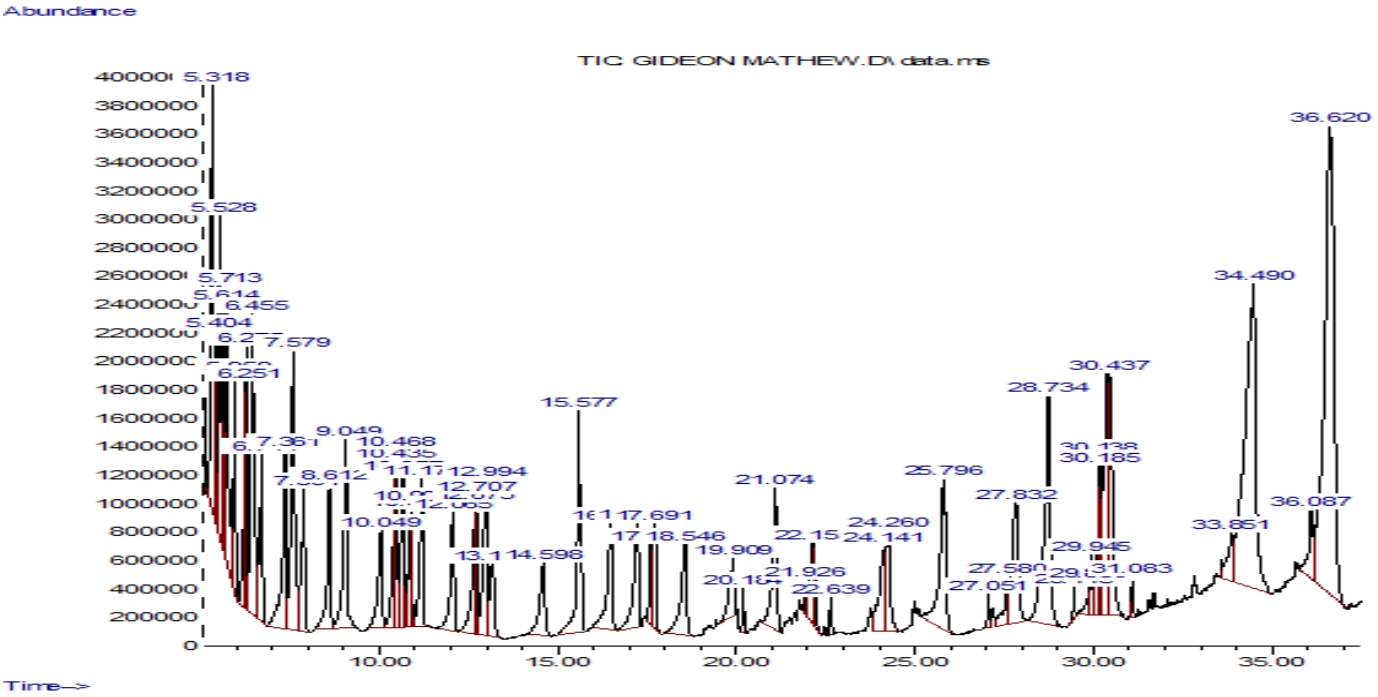

Figure 2. Chromatogram of the phytochemicals present in the prepared sample

Oleic Acid is the major component (13.04 %) identified at a retention time of 36.62 min, followed by1,1,1,3,5,5,7,7,7-Nonamethyl-3-(trimethylsiloxy)tetrasiloxane (9.50 %) at retention time 34.49 min, 9-Heptadecanone (3.72 %) at retention time 28.73 min, Cystamine (3.35 %) at retention time 5.31 min, Tetrahydro-4H-pyran-4-ol (3.15 %) at retention time 6.45 min, and Acetic acid, [(aminocarbonyl)amino (3.13 %) at retention time 7.57 min, cycloeicosane (3.03 %) at retention time 30.38 min, 3-Propoxyamphetamine (2.83 %) at retention time 25.79 min, 1-Docosene (2.68 %) at retention time 30.43 min, 4-amino-1-Pentanol (2.46 %) at retention time 5.52 min, dodecamethyl- Cyclohexasiloxane, (2.46 %) at retention time 15.57 min, Alanyl-.beta.-alanine, TMS derivative (2.36 %) at retention time 27.83 min, 1,2,5-Oxadiazol-3-carboxamide, 4,4'-azobis-, 2,2'-dioxide (2.03 %) at retention time 21.07 min. The remaining consponents were present in proportions of less than 2%.

The components names, area percent, retention times, and molecular weights are summarized in Table 1. Figure 2 shows the spectrum of the relative abundances of the phytochemicals against their retention time.

Table 1.0. Phytochemicals obtained from the prepared sample

Pk#	RT	Area%	Compound Name	Molecular Weight
1	5.318	3.35	Cystamine	152.0
2	5.404	0.98	2-methyl- Piperazine,	100.0
3	5.528	2.46	4-amino-1-Pentanol,	103.0
4	5.614	1.20	2-Isopropoxyethylamine	104.0
5	5.959	1.42	N-Methoxy-1-ribofuranosyl-4-imidazolecarboxylic amide	155.0
6	6.275	0.73	1,2,5-Oxadiazol-3-carboxamide, 4,4'-azobis-, 2,2'-dioxide	284.0
7	6.455	3.15	Tetrahydro-4H-pyran-4-ol	102.0
8	6.711	1.34	8-[N-Aziridylethylamino]-2,6-dimethyloctene-2	224.0
9	7.361	1.94	3,3-dimethyl-4-(1-aminoethyl)- Azetidin-2-one	142.0
10	7.579	3.13	Acetic acid, [(aminocarbonyl)amino	132.0
11	7.891	1.37	5-methyl-2-Heptanamine,	128.0
12	8.612	1.42	2-chloro-Acetamide,	93.0
13	9.049	1.95	N-methyl-1-Octadecanamine,	283.0
14	10.049	1.18	hydroxy[(1-oxo-2-propenyl)amino]- Acetic acid,	145.0
15	10.468	0.68	2-Formylhistamine	138
16	10.657	1.35	3,4-dibenzyloxy -2-fluoro-.beta.-hydroxy-N-methyl- Benzeneethanamine,	381.0
17	10.874	0.80	[S-(R*,R*)]-1,2,3,4-Butanetetrol	122.0
18	10.901	0.42	Tetraacetyl-d-xylonic nitrile	343.0
19	11.178	1.40	N,N-Dimethyl-dimethylphosphoric amide	121.0
20	12.065	1.36	dl-Phenylephrine	167.0
21	12.673	1.13	2,5-difluoro-.beta.,3,4-trihydroxy-N-methyl- Benzeneethanamine,	219.0
22	12.994	1.74	Ethyl oxamate	117.0
23	14.598	1.16	Cystine	240.0
24	15.577	2.46	dodecamethyl- Cyclohexasiloxane,	429.0
25	16.470	1.62	Chlorodifluoroacetamide	129.0
26	17.241	1.53	3,4-dibenzyloxy-2-fluoro-.beta.-hydroxy-N-methyl- Benzeneethanamine	381.0

27	17.606	0.53	2-methyl- Octadecane,	268.0
28	17.691	0.98	N-(2-amin oethyl)- 1-hexadecanesulfonamide,	349.0
29	8.546	1.56	N-methyl-1Benzeneethanamine,	135.0
30	19.909	0.85	2-fluoro-2',4,5- trihydroxy-N-methyl- Benzenethanamine,	201.0
31	20.184	0.23	Pentadecane	212.0
32	21.074	2.03	1,2,5-Oxadiazol-3-carboxamide, 4,4'-azobis-, 2,2'-dioxide	284.0
33	21.926	0.20	Hexadecane	226.0
34	22.127	0.73	Metaraminol	167.0
35	22.155	0.55	2-(2-aminopropoxy)-3-methyl- Benzenemethanol,	195.0
36	24.141	1.30	13-Tetradecen-1-ol acetate	254.0
37	24.260	1.33	10-Methyl-E-11-tridece-1-ol acetate	254.0
38	25.796	2.83	3-Propoxyamphetamine	193.0
39	27.051	0.20	Z-8-Hexadecene	224.0
40	27.580	0.56	N-(3-aminopropy l)- 1,4-Butanediamine,	145.0
41	27.832	2.36	Alanyl-.beta.-alanine, TMS derivative	233.0
42	28.734	3.72	9-Heptadecanone	254.0
43	29.445	0.12	Hexadecanoic acid, methyl ester	270.0
44	29.859	0.27	4-Cyclohexene-1,2-dicarboxylic acid, 4-chloro-, bis(trimethylsilyl) ester	333.0
45	29.945	0.47	Dibutyl phthalate	278.0
46	30.138	0.99	9-Eicosene, (E)-	280.0
47	30.185	0.80	1-Tridecene	182.0
48	30.385	3.03	Cycloeicosane	280.0
49	30.437	2.68	1-Docosene	308
50	31.083	0.16	9-Octadecenoic acid (Z)-, methyl ester	296.0
51	34.490	9.50	1,1,1,3,5,5,7,7,7-Nonamethyl-3-(trimethylsiloxy)tetrasiloxane	369.0
52	36.087	0.78	3,7,11-trimethyl- 2,6,10-Dodecatrien-1-ol,	222.0
53	36.620	13.04	Oleic Acid	264.0

From Table 1, the phytochemical Oleic Acid, 1,1,1,3,5,5,7,7,7-Nonamethyl-3-(trimethylsiloxy)tetrasiloxane, 9-Octadecenoic acid (Z)-methyl ester, 1-Docosene, Cycloeicosane, 1-Tridecene, 9-Eicosene, Pentadecane, (E)-, Dibutyl phthalate, Hexadecane, 13-Tetradecen-1-ol acetate, 10-Methyl-E-11-tridece-1-ol acetate, Z-8-Hexadecene, Alanyl-.beta.-alanine, TMS derivative, 9-Heptadecanone, Hexadecanoic acid, methyl ester, N,N-Dimethyl-dimethylphosphoric amide, dodecamethyl- Cyclohexasiloxane and 2-methyl- Octadecane are phytochemicals initially present in *C. procera* extract of different solvents [15-19], although some still maintain their parent name but undergo few changes or shift in their substituent(s) and or functional group(s). 2-methyl-Piperazine, N-Methoxy-1-ribofuranosyl-4-imidazolecarboxylic amide, 1,2,5-Oxadiazol-3-carboxamide, 4,4'-azobis-, 2,2'-dioxide, 8-[N-Aziridylethylamino]-2,6-dimethyloctene-2 and 3,3-dimethyl-4-(1-aminoethyl)- Azetidin-2-one are phytochemicals that might originated from the antibiotic used [24].

New phytochemicals such as Cystamine, [S-(R*,R*)]-1,2,3,4-Butanetetrol, Cystine, dl-Phenylephrine, Metaraminol, N-methyl-1Benzeneethanamine, 3-Proproxyamphetamine were observed, which is due to the synthetic reaction initiated by heat and concentrated sulfuric acid [25], others such as 2,5-difluoro-beta.,3,4-trihydroxy-N-methyl-Benzeneethanamine, Benzeneethanamine, 3,4-dibenzyloxy-2-fluoro-.beta.-hydroxy-N-methyl-Benzeneethanamine, 2-fluoro-2',4,5-trihydroxy-N-methyl- Benzenethanamine, 2-(2-aminopropoxy)-3-methyl- Benzenemethanol and 4-Cyclohexene-1,2-dicarboxylic acid, 4-chloro-,

bis(trimethylsilyl) ester are complex organic compound formed from the reaction, while the remaining are compounds with substituents and functional groups transformation which is challenging to identify if their source is from either the plant extract or antibiotic used.

3.2. Antimicrobial screening of the prepared sample.

The antimicrobial screening of the prepared sample was carried out on two bacterial strains of *S. aureus*, and *Salmonella spp* as shown in Table 2. The bacteria strains showed resistance to *C. procera* extract at 5 mg/mL, and to Ampicillin at 1 mg/mL, the resistance is due to the resistant nature of the bacteria isolates and the low concentration of the plant extract and the antibiotic used [2]. On the other hand, the prepared sample at 100 µg/mL successfully inhibit the growth of *S. aureus*, and *Salmonella spp* with inhibition zones (ZOI) of 16.8 mm and 21.4 mm respectively. This result obtained is consistent with those reported in a previous study, where the addition of sulfuric acid in a mixture of plant extract and antibiotic increased the zone of inhibition against resistant clinical isolates of *Streptococcus* spp. (HVS), *Salmonella* typhi (stool), *E. coli* (urine), *Shigella spp*. (stool), and *S. aureus* (HVS) [1]. Similarly, another study [2] also reported an increase in the zone of inhibition for resistant *Salmonella spp*. following the addition of sodium hydroxide followed by sulfuric acid in the mixture of plant extract and aspirin, and is also in line with [3] where, at 0.1 mg/mL, Guava Aspirin Guava GAG, combination inhibited the growth of *E. coli* and *Streptococcus spp*, with a zone of inhibition of 5.0 mm while, Guava Guava, GG extract reaction with concentrated sulfuric acid at 0.1 mg/mL inhibited the growth of *E. coli*, *S. aureus Salmonella spp*, and *Streptococcus spp.* with inhibition zones of 12.0 mm, 7.0 mm, 9.0 mm, and 10.0 mm, respectively.

Table 2. Zone of inhibition (mm) of resistant bacterial strains in response to prepared samples

	Samples		
Bacteria	***C. Procera* Extract**	**Ampicillin cloxacillin**	**Prepared sample**
	5 mg/mL	**1 mg/mL**	**100 µg/mL**
Salmonella spp	0 mm	5.3 mm	21.40 mm
Staphylococcus Aureus	0 mm	0 mm	16.80 mm

The growth inhibition of the resistant bacteria observed is due to the presence of the new and transformed bioactive compounds present in the mixture, they act in synergism with some of the phytochemicals initial present in *C. procera* extract to increase the mixture antimicrobial activities, as Cystamine (functionally related to a cysteamine) figure 3, plays a role as an EC 2.3.2.13 (protein-glutamine gamma-glutamyltransferase) inhibitor and it may also protect against liver damage [26]. 4-Amino-1-pentanol figure 4, is reported to show anticancer activity, antiherpetic properties, inhibiting viral replication and preventing HSV from entering cells [27]. 2-(3-Propoxyphenyl)ethanamine figure 8, also known as 3-Propoxyamphetamine, is a psychoactive drug, however, it has also been studied for its potential therapeutic effects in medical research [28]. 1-Docosene has been found to have antibacterial, antifungal, and anti-inflammatory activities [29]. Oleic acid, figure 10, being the most abundant phytoconstituent in the sample, is an octadec-9-enoic acid which has a role as an EC 3.1.1.1 (carboxylesterase) inhibitor, an Escherichia coli metabolite, a plant metabolite, a Daphnia galeata metabolite, an antioxidant and a mouse metabolite [30-31]. dl-Phenylephrine figure 6, is used for temporary relief of stuffy nose, sinus, and ear symptoms caused by flu, common cold, allergies, or other breathing illnesses (such as sinusitis, bronchitis) [32]. Hexadecnoic acid, octadecanoic acid, methyl ester possess some antioxidant, anti-inflamatory and

antimicrobial activity [33]. N-Methoxy-1-ribofuranosyl-4-imidazolecarboxylic amide, 1,2,5-Oxadiazol-3-carboxamide, 4,4'-azobis-, 2,2'-dioxide and 1,2,5-Oxadiazol-3-carboxamide, 4,4'-azobis-, 2,2'-dioxide are imidazole derivatives, imidazole derivatives are reported to show (i) antibacterial activity; (ii) anticancer activity; (iii) antitubercular activity; (iv) antifungal; (v) analgesic activity; (vi) anti-HIV activity [34].

Aramine (metaraminol) figure 5, is indicated for prevention and treatment of the acute hypotensive state occurring with spinal anesthesia, as adjunctive treatment of hypotension due to hemorrhage, reactions to medications, surgical complications, and shock associated with brain damage due to trauma or tumor [35-36]. 3,3-dimethyl-4-(1-aminoethyl)- Azetidin-2-one, was shown to have good antimicrobial activity [37]. Cystine, figure 9, is required for proper vitamin B6 utilization, helpful in burns and wound healing, breaks down mucus deposits in illnesses such as bronchitis as well as cystic fibrosis, assists in the supply of insulin to the pancreas, it also increases glutathione levels in the liver, lungs kidneys and bone marrow [38]. Methamphetamine (chemically similar to amphetamine), is used to for the treatment of attention-deficit hyperactivity disorder (ADHD) and narcolepsy, a sleep disorder [39]. 3,7,11-trimethyl- 2,6,10-Dodecatrien-1-ol, (Farnesol) figure 7, has been reported to exhibit anti-cancer and anti-inflammatory effects, and also alleviate allergic asthma, gliosis, and edema [40].

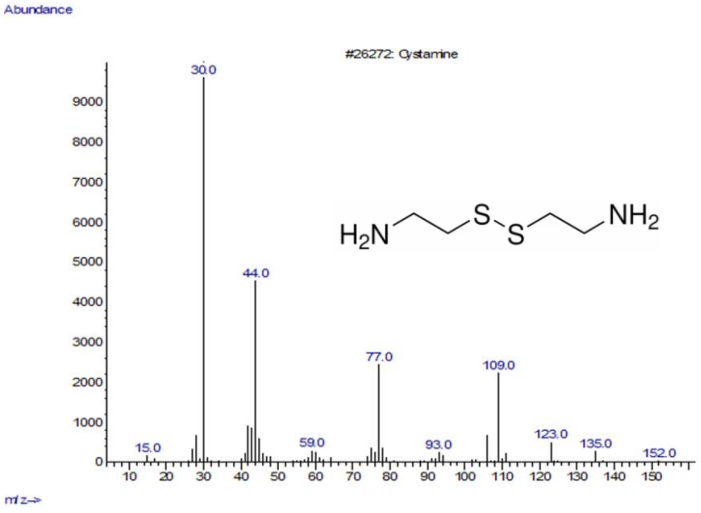

Figure 3. Spectrum and structure of Cystamine.

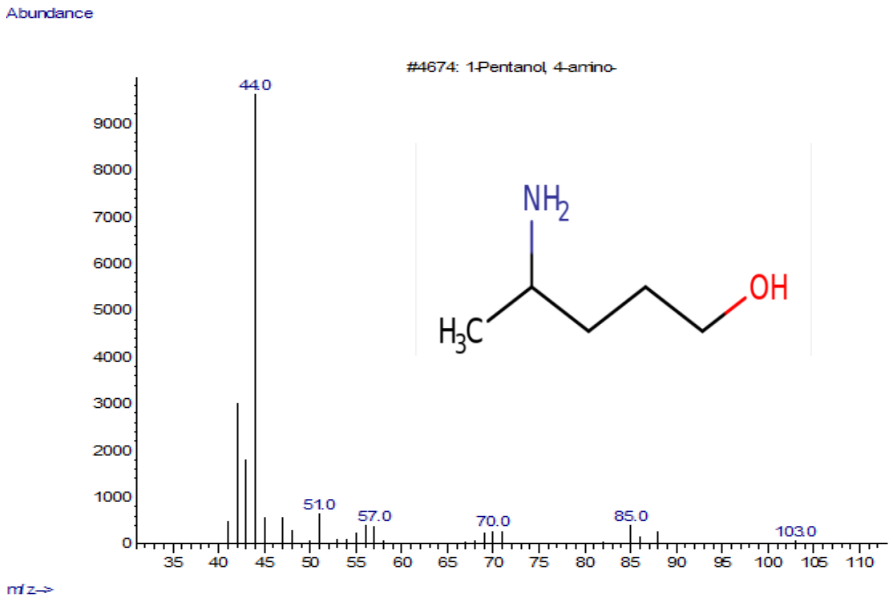

Figure 4. Spectrum and structure of 4-amino-1-pentanol.

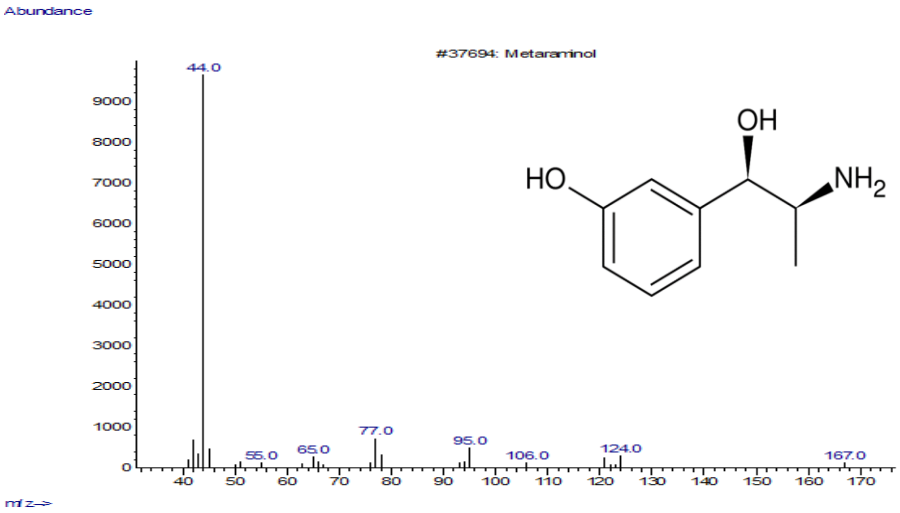

Figure 5. Spectrum and structure of Metaraminol.

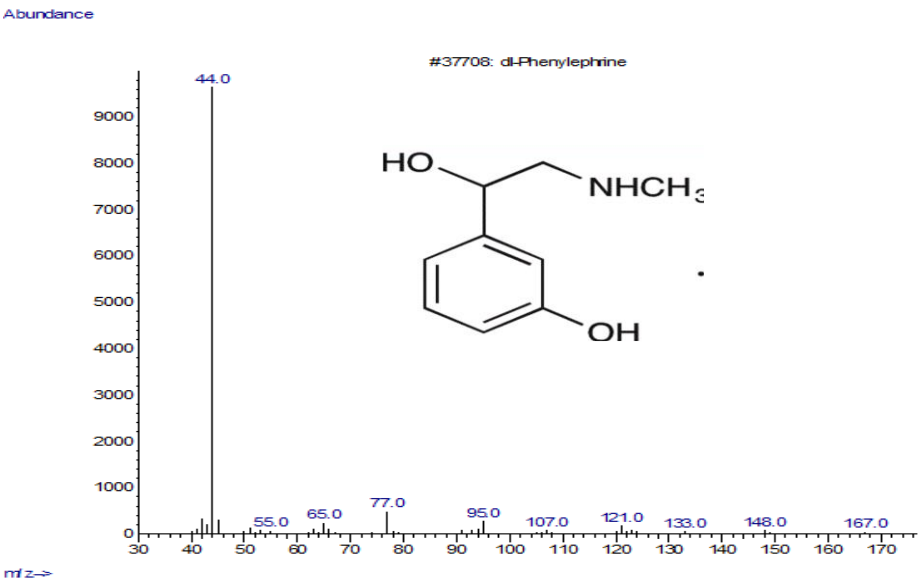

Figure 6. Spectrum and structure of dl-phenylephrine.

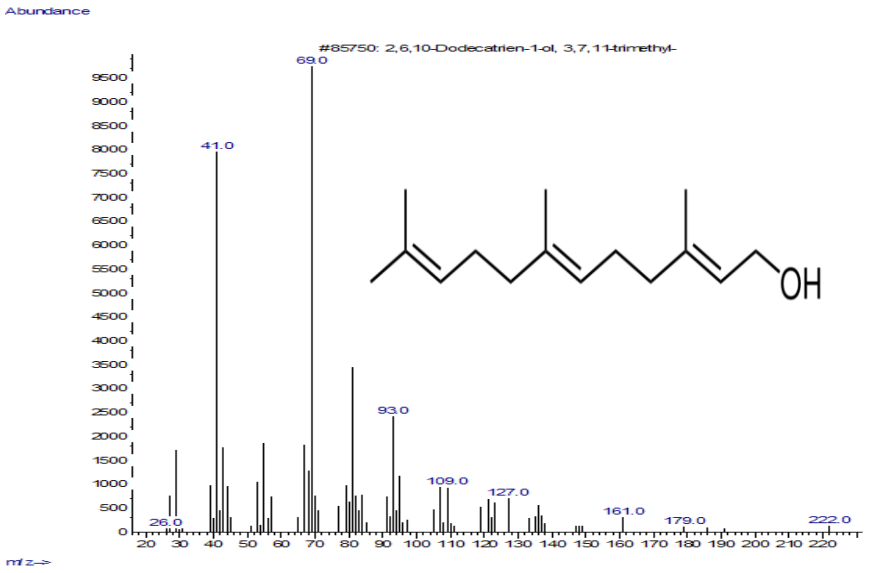

Figure 7. Spectrum and structure of Farnesol.

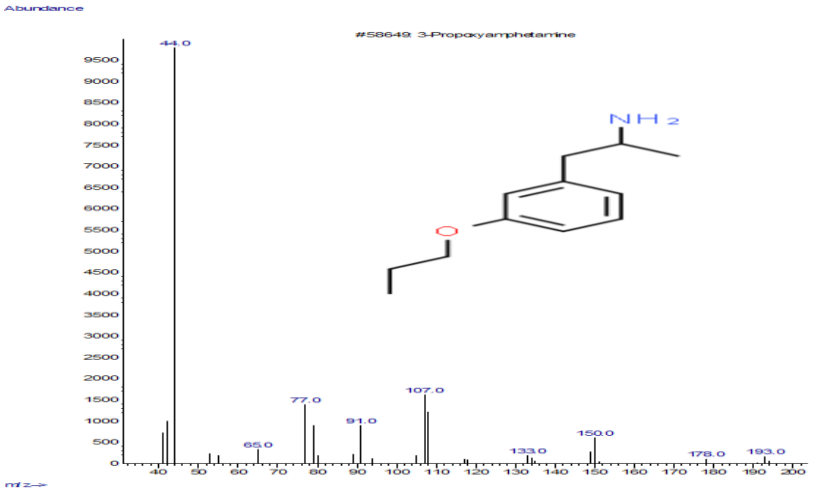

Figure 8. Spectrum and structure of 3-Propoxyamphetamine.

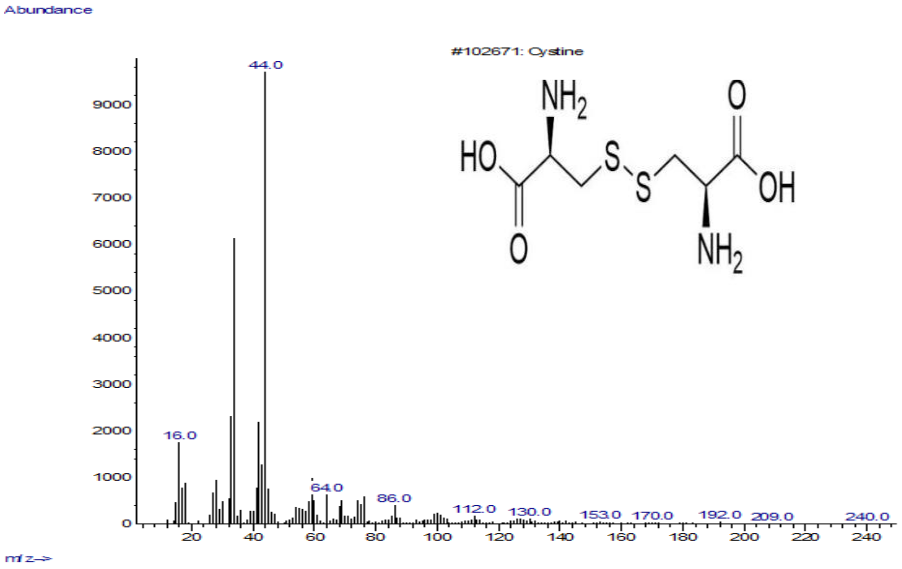

Figure 9. Spectrum and structure of Cystine.

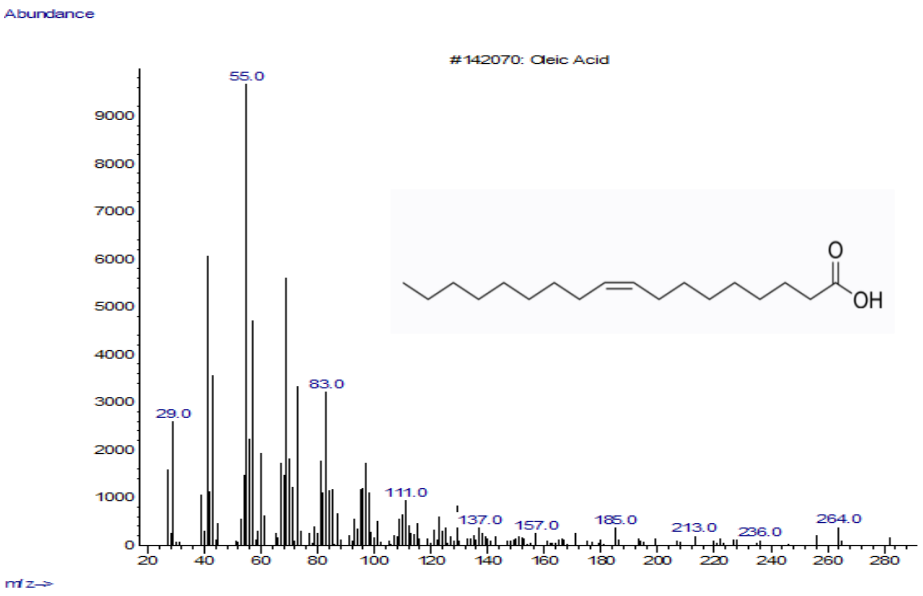

Figure 10. Spectrum and structure of Oleic.

CONCLUSION

This study present a simple, basic and eco-friendly method of which the antimicrobial activity of two less effective antimicrobial agents can be improved through synergism to inhibit the growth of resistant clinical bacteria isolates. The prepared sample highly susceptible to resistant S. aureus moving the ZOI from 0 mm to 1 mm, also moving the ZOI of resistant Salmonella spp from 5.1 mm to 21.4 mm. GC-MS analysis reveals the presence of 53 phytochemicals, the five (5) most abundant are oleic acid 13.04 %, 1,1,1,3,5,5,7,7,7-Nonamethyl-3-(trimethylsiloxy)tetrasiloxane 9.50 %, 9-Heptadecanone 3.75%, Cystamine 3.35 % and Tetrahydro-4H-pyran-4-ol 3.15 %. Eighteen (18) out of the 53 phytochemicals were reported to have known biological activities thus, some undergo molecular transformation to a new molecule and/or an analogue to the existing biologically active compound due to the reaction condition used. Three of the phytochemicals present were reported to exhibit anticancer properties (Farnesol, 4-amino-1-pentanol and the of imidazole derivative similar to the drug Ribavir).

The results of this works reveals that medicinal plants phytochemicals can be used in synthetic combination reactions with themselves or other drugs or reagents to produce vast array of compounds with good pharmacological activities or compounds which can be used as starting materials, intermediates or derivatives in pharmaceutical productions.

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