Special Edition on "Frontiers of Biosciences in Sustainable Development (FBSD)"
CIBTech Journal of Zoology ISSN: 2319–3883; http://www.cibtech.org.htm
2023 Vol.12/S1, pp.173-194/Mohanasundari et al
***Research Article** (Open Access)*

EFFECTS OF *ILLICIUM VERUM* HOOK.F EXTRACT ON DRUG RESISTANT BACTERIA AND ESTIMATION OF ITS ANTIOXIDANT EFFICACY

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ABSTRACT
Our present study investigated the phytochemical constituents of *Illicium verum*, a Chinese herb well known for its culinary significance and medicinal properties for more than 3000 years. *I.verum* extracts of three different solvents, diethyl ether, methanol and hexane were screened for potential secondary metabolites. Amongst the three, methanol extract established the highest yield of bio active compounds like phenols, tannins, flavonoids, saponins anthocyanin, carbohydrates, coumarins, terpenoids, steroids, glycosides, quinones, terpenoides followed by diethyl ether and hexane extracts. As methanol extract was rich in flavonoids, tannins followed by phenols and other phytocompounds, it was tested for antibacterial efficacy against clinical pathogens like *E. coli, K. pneumoniae, P. mirabilis and S. aureus* and also analyzed its antioxidant activity. Different concentrations of methanol extracts of *I. verum* like 20 µg/ml, 40 µg/ml and 80 µg/ml demonstrated a significant inhibitory action against all the chosen pathogens and remarkably against *E. coli* and *S. aureus*. Methanol extract of *I.verum* was also subjected for free radical scavenging by DPPH assay, which displayed an exceptional antioxidant activity. The phytochemicals of methanol extract were analyzed by Gas Chromatography-Mass Spectrometry (GCMS) which revealed Estragole, Benzene, 2.1-methoxy-4-(1-Propenyl), Anetholes, Phenolic compounds, Sesquiterpenes, Benzene acetic acid, Alpha hydroxy-4 methoxy, Benzene acetic acid, Alpha hydroxy-2-methoxy and Anisoles. These findings indicate that *I. verum* is *ri*ch in phytochemicals with antibacterial and antioxidant activity that could be explored more in the development of novel antibiotics and natural antioxidants to be used in various lifestyle disorders and in the food industry suppressing the oxidative deterioration.

Keywords: *Illicium verum, Phytochemicals, GC-MS, Antibacterial activity, Antioxidant activity.*

INTRODUCTION

The current scenario of population explosion, challenged employment opportunities, poor sanitation and dietary intake of low-quality foods such as canned, tinned and other processed ready meals with feed additives. Consumption of synthetic preservatives and antioxidants, sugar, salt and fat more than the recommended quantity has led to chronic infectious diseases and lifestyle disorders. Continuous emergence of diseases, directed us to overuse of antibiotics that has become indispensable in disease control and treatment, despite the increase in multidrug resistant pathogens and antibiotic residues in the food chain (Yu *et al*., 2020). Use of synthetic antioxidants in food preservation to prohibit microbial growth and oxidation of fat poses a serious threat causing lifestyle disorders in man (Gupta and Sharma, 2006). Emergence of multi drug resistant bacteria and accumulation of its antibiotic residue in the environment lead to significant morbidity and mortality in human population cause an alarming threat to global health leading to an intense economic stress (Centers for Disease Control and Prevention, 2019), which eventually demands a continuous attention of their identification and challenges the development of potential novel antibiotics to treat them (Terreni *et al.*, 2021; Koulenti *et al.*, 2020; Fischbach *et al.*, 2009). Increased harmful effects of synthetic antimicrobial drugs and a search for an alternate treatment method threw light on bio active components of plants with curative characteristics and have no side effects even if used in chronic conditions eventually opened more avenues like phytotherapy, ethnopharmacology, siddha and ayurveda (Suntar, 2020; Wiart, 2007; Duke, 1992). Secondary metabolites like carotenoids, quinones, coumarins, alkaloids, terpenoids, phenols, flavonoids and tannins have significant pharmacological importance with wide range of therapeutic values like anti-inflammatory, antibacterial, antioxidant properties etc. (Mbaveng *et al.*, 2015; Mendoza *et al.*, 2018; Anand *et al.*, 2019; Anand *et al.*, 2020; AlSheikh *et al.*, 2020; Mohammed *et al.*, 2021). Since the ancient period of time herbs and spices like turmeric , ginger, garlic, clove, cinnamon, elaichi, pepper, cilantro and ajwain cumin, coriander, basil, star anise have established a special place in our diet not only for their unique flavor and aroma but also as therapeutic agents like antioxidants and anti-aging (Forni *et al.*, 2019; Guan *et al.*, 2021; Engwa,2018), immunomodulators (Behl *et al.*, 2021; Mohanasundari *et al.*, 2022; Musthafa *et al.*, 2018), anticancer (Choudhari *et al.*, 2020), antiviral (Zhang *et al.*, 2012; Biswas *et al.*, 2020; Chojnacka *et al.*, 2020; Ben-Shabat *et al.*, 2020), neuroprotective (Velmurugan *et al.*, 2018), antimicrobial (Ayaz *et al.*, 2019), antidiabetic (Bacanli *et al.*, 2019), antifungal (Makhuvele *et al.*, 2020), anti-infectious and immune boosters (Lillehoj *et al.*, 2018; Umakanth *et al.*, 2020).

Star anise, an evergreen, medium-sized tree widely distributed throughout Asia, China and Vietnam with star-shaped fruit (Loi *et al.*, 1970), belongs to the genus Illicium and the family Schisandraceae (Reveal *et al.*, 2011; Simpson *et al.*, 2005). *I.verum* Chinese herb known for its traditional medicinal properties like antioxidant, antibacterial, antiviral, antifungal, antihelminthic, insect killing, secretolytic, induce response against toxic stimuli, anti-inflammatory, analgesic, proton pump inhibiting, sleep promoting, to clear sputum in cough, as muscle relaxant and estrogenic effects (Patra *et al.*, 2020; Padmashree *et al.*, 2007). Star anise is well attributed for its rich polyphenols, tannins and flavonoids, widely used in Chinese medicine for treating rheumatic pain, skin problems, sleep disorders, stomach aches and vomiting (Itoigawa *et al.*, 2004; Chinese Pharmacopoeia Commission, 2010). Ethanol and Supercritical CO_2 extracts of leaves and twigs of *I. verum* exhibit wider and powerful antibacterial property against the bacteria like *A. baumannii*, *S. aureus* and *P aeruginosa* (Yang *et al.*, 2021) also against the *E. coli*, *Streptococcus sp.*, *Bacillus sp.*, *Pseudomonas sp.*, more remarkably than *Cuminum cyminum* (Balaram *et al.*, 2021). Essential oil of *I. verum* works effective against MRSA clinical isolates from nosocomial diseases and *Acinetobacter baumannii* a major human pathogen causing hospital-acquired infections and able to scavenge free radicals, inhibit protein denaturation and lipid peroxidation (Luis *et al.*, 2019; Muhsinah *et al.*, 2022). Antifungal property of Star anise can be used in preservation of fruits and vegetables against fungal infections (De *et al.*, 2002; Wang *et al.*, 2007; Huang *et al.*, 2010; Wang *et al.*, 2011; Zhang *et al.*, 2015; Aprotosoaie *et al.*, 2016;). It is also reported for the first time that a fish diet supplemented with *I. verum* in *Catla catla* has influenced a better growth performance and improved immune response and disease resistance against *Aeromonas hydrophila* which causes Septicemia, a dreadful disease (Mohanasundari *et al.*, 2022).

Established through various extraction of *I.verum* that Anethole, a phenylpropanoid is the chief constituent of *I. verum* responsible for its unique taste and smell with antibacterial and antifungal properties (Cu *et al.*, 1990; Song *et al.*, 2007) and (Patra *et al.*, 2020; Ohira *et al.*, 2009)

GC-MS ANALYSIS

GC-MS analysis was done by injecting 1µL of extract into the GC-MS (Clarus 680 GC) and Helium Gas flowing at a rate of 1 ml/min constantly separated the components. The temperature of the oven was maintained for 2 minutes at 60°C; and gradually increased the temperature at the rate of 10 °C /min to 300°C for 6 minutes. In the mass detector the transfer line and ion source temperature were maintained at 240°C.The electron impact at ionization mode was 70eV for a scan time of 0.2 sec with a regular interval of 0.1 sec. GC-MS NIST 2009) have determined that the ethanol extract of *I. verum* has two main antiviral therapeutic components namely Illiverin and Illicinone and (Yang *et al.*, 2012) has reported that *I.verum* has shikimic acid , an important component used in the preparation of antiviral medicine Tamiflu for flu infections in abundance. (Aly *et al.*, 2016) also reported that ethyl ether and ethyl acetate extracts displayed low IC_{50} values, eventually a significant antioxidant activity. Similarly, samples of essential oil, ethanol and methanol extracts of *I. verum* exhibited a remarkable antioxidant activity equivalent to synthetic antioxidant BHT at the concentration of 10 mg/ml (Yang *et al.*, 2012). Studies show that SEE and CEE of *I. verum* exhibit an excellent antioxidant property and their constituents like tannins, terpenoids, cardiac glycosides, flavonoids, oil and phenols play an important role for the same (Yu *et al.*, 2021). Studies of (Cu *et al.*,1990; Song *et al.*, 2007; De Castro *et al.*, 2010) have recorded that the composition of star anise essential oil includes estragole anethole, anisyl aldehyde, limonene, anisyl acetone, terpineol, anisyl alcohol, phellandrene and various other phyto components responsible for its therapeutic uses. Thus, with the thorough knowledge of references made we screened phytochemicals of three different extracts of *Illicium verum* viz. diethyl ether, methanol and hexane. As methanol extract exhibited a significant level of potential bioactive components compared to that of diethyl ether and hexane it was extended for GC-MS study to understand the array of bioactive molecules that could be responsible for various medicinal properties of *Illicium verum.* In the year 2017 WHO enlisted about 12 families of bacteria that pose a serious threat on human health and continuous emergence of multi drug resistance alarmed the scientist community to search for new antibiotics (Yu *et al.*, 2020). With the view of WHO, as priority pathogens we have chosen four clinical isolates, *E. coli*, *K. pneumoniae*, *P. mirabilis* and *S. aureus* for our investigation on antibacterial activity of *I. verum.* and also analyzed its antioxidant property.

MATERIALS AND METHODS

Preparation of plant extracts

I.verum fruits procured from the market were shade dried, ground in a mixer and sieved with a 2 mm diameter mesh. 20 g of well dried herb fine powder was successively extracted with 250 ml of organic solvent (Diethyl ether, Methanol and Hexane) by Soxhlet apparatus (72 h ;40-50º C). After that, under vacuum conditions all the extracts were concentrated in a rotary evaporator to obtain crude extracts, which were then dried and kept in a desiccator until needed (Lopez-Bascon and De Castro, 2020; Trease and Evans,1989). The dried fraction was then evaluated for further analysis like phytochemical screening, GC-MS study, antibacterial activity and antioxidant property.

Screening for phytochemicals

Qualitative analysis of all the three different extracts of *I. verum* were performed, adopting standard methodologies as explained by (Trease and Evans,1989; Harborne, 1973; Sofowora, 1993; Savithramma *et al.*, 2011) to screen the bioactive secondary metabolites. The presence of acids was confirmed by Millon's reagent test and alkaloids by Mayer's test. Occurrence of anthocyanins, betacyanins and coumarins were confirmed by Sodium hydroxide test, carbohydrates by Anthrone test. Presence of phenolic compounds, cardiac glycosides and tannins were evaluated by Ferric chloride test. Flavonoids, glycosides and quinones were revealed by sulphuric acid test. Iodine test confirmed the presence of terpenoids, steroids and starch and biuret test confirmed the proteins. Froth test was used to detect saponins.

Microorganisms for testing

Clinical isolates of test microorganisms namely, (G -) *Esherichia coli* (ATCC 25911) (G -) *Klebsiella pneumoniae* (ATCC 700603) (G -) *Proteus mirabilis* (ATCC 12453) and (G +) *Staphylococcus aureus* (ATCC 25923) was obtained from The King Institute of Preventive Medicine and Research, Chennai, Tamilnadu. All the cultures were maintained and sub-cultured using Mueller Hinton broth (MHB) at 37^0C on rotary shaker at 200 rpm for 24 hrs.

Disc diffusion assay

Methanol extract of *I.verum* was subjected to Disc diffusion assay to analyze the antibacterial property (Bauer et al.1966). 20 ml of sterile Muller Hinton Agar (MHA) medium poured in petri plates were kept ready for inoculation. Strains were swabbed uniformly on the individual agar plates using sterile cotton. A 6 mm paper disc prepared from Whatmann's no.1 filter paper with the help of a disc cutter was sterilized by autoclaving at 15 lbs pressure for 15 minutes under aseptic conditions. After sterilization, discs were impregnated with 20, 40 and 80 µg/ml of methanol extract and 5 µg/ml of Ampicillin (Standard) were placed in four different places on a petri plate. The petri plates were maintained at room temperature for 24 hours in an incubator. The zones of inhibition were studied, measured and expressed their diameters in millimeters. This assay was done in 5 replicates and their mean values represent the results.

DPPH-Antioxidant assay

The efficacy of antioxidant activity (AA %) of different concentrations of methanol extracts of *I. verum* (20, 40 and 80 µg/ml) were assessed by the ability of 1,1-diphenyl-2-picrylhydrazyl (DPPH) radicals. According to the methodology described by (Brand-Williams *et al.*,1995) the radical scavenging activity was conducted and measured. Under stable conditions, the 0.5 ml of samples were made to react with a reaction mixture consisting 0.3ml of DPPH radical solution mixed in 0.5 ml of ethanol with 3 ml of absolute ethanol. As antioxidant compounds have the ability to donate hydrogen, they bring out a reduction reaction when made to react with DPPH. The reaction is indicated by a color change from deep violet to light yellow after 100 minutes; it was inferred at 517 nm in UV-VIS spectrophotometer (UV-10 Thermo).

Radical scavenging activity in percentage (AA %) was estimated using the formula given below as explained by (Brand-Williams *et al.*,1995; Mensor *et al.,* 2001).

$$1\ \% = \left[1 - \frac{X1\text{-}X2}{X3} \right] \times 100\%$$

where,

X1 = Absorbance of he tested samples with DPPH

X2= Absorbance of the tested samples without DPPH

X3 = Absorbance of the control sample

IC_{50} value denotes the concentration of the tested samples that results in 50% of inhibition.

STATISTICAL EXPRESSION

Analysis of variance (ANOVA) using SPSS version (19.0) was carried out for the results obtained and were expressed as mean ± standard error (SE).

RESULTS

Phytochemical screening

Phytochemical screening of diethyl ether, methanol and hexane extracts of *I. verum* revealed an array of bioactive components like alkaloids, quinones, coumarins, carbohydrates, steroids acids, cardiac glycosides, betacyanin, anthocyanin, terpenoids, flavonoids, saponins, phenols and tannins. The results establish that methanol extract has revealed more potential bio active components followed by diethyl ether and hexane extracts. All the three extracts confirmed the presence of flavonoids, terpenoids and tannins. Flavonoids and tannins are significantly higher in methanol extract than the other two extracts. Carbohydrates and saponins are present in diethyl ether and methanol extract but slightly higher in methanol extract and absent in hexane extract. Similarly, anthocyanin is present in methanol and hexane extracts but absent in diethyl ether. Only methanol extract revealed the presence of coumarins, glycosides, phenols, quinones and steroids. Alkaloids are present in diethyl ether and hexane extract but absent in methanol. Starch is found to be present only in diethyl extract and absence of acids, cardiac glycosides and proteins in all the three extracts (Table 1).

GC-MS analysis

GC-MS study of methanol extract of *I. verum* in our investigation revealed the following compounds,Estragole(1.382%),Benzene,2.1-methoxy-4-(1-Propenyl)-(5.353%), Anetholes- 1H-Indenol,2,3-Dihydro,(88.421%), Phenolic compounds, Alpha-bergamotene is a sesquiterpene polycyclic olefin Bicyclo [3.1.1]Hept-2-ene,2,6-Dimethyl-6-(4-methyl-3-pentenyl)--(0.541%) , Benzene acetic acid, Alpha hydroxy-4 methoxy(0.821%), Benzene acetic acid, Alpha hydroxy-2-methoxy (0.495%), Anisole 1-(3-Methyl-2-Butenoxy)-4-(1-Propenyl)Benzene (2.988%) foeniculin phenol ethers. (Table2)(Fig 1)

Antibacterial Assay

As the methanol extract of *I. verum* exhibited the presence of phytochemicals significantly higher than the extracts of diethyl ether and hexane, methanol extract in different concentrations and the antibiotic ampicillin as positive control were taken for further study to analyze the antibacterial activity against the chosen clinical isolates such as *E. coli*, *K. pneumoniae*, *P. mirabilis* and *S. aureus* and assessed by the zone of inhibition. All the different concentrations of methanol extract of *I. verum* showed inhibitory effects on all bacteria, similar to that of antibiotic, Ampicillin (Fig.2). At 20 µg/ml concentration, methanol extract has revealed the maximum antibacterial activity against *E. coli* (6 mm) secondly against *S. aureus* (4 mm), *P. mirabilis* (3 mm) and *K. pneumoniae* (2 mm). The mid-concentration, 40 µg/ml exhibited a slightly higher inhibitory effect against all the test microorganisms than the 20 µg/ml. The zone of inhibition was maximum against *E. coli* (7 mm) trailed by *S. aureus* (5 mm), and significantly lesser effect against *P. mirabilis* (4 mm) and *K. pneumonia*e (3 mm). And the control was recorded as 10 mm. A significant strong antibacterial efficacy of *I. verum* was established at the highest concentration of Methanol extract, 80 µg/ml employed in the present study. The maximum size of zone of inhibition was recorded against *E. coli* (8 mm) followed by *P. mirabilis* and *S. aureus* (6mm) and minimum against *K. pneumoniae* (4 mm) whereas Ampicillin at standard concentration of 5 µg/ml showed a slightly a different pattern as 11mm in *E. coli* followed by 10 mm in *P. mirabilis*,8 mm in *S. aureus* 4mm in *K. pneumoniae*. Fig. 3 represents the mean values of triplicates of antibacterial activity. Thus, the overall results suggest that a higher concentration of *I. verum* as an antibacterial agent can challenge the synthetic antibiotics and could be developed as a novel non-hazardous antibiotic from a natural source to serve mankind.

Table 1 Phytochemical analysis of different solvent extracts of *Illicium verum*

No	**Phytocompounds**	***Diethyl ether***	***Methanol***	***Hexane***
1	Acid	-	-	-
2	Alkaloids	+	-	+
3	Anthocyanin/Betacyanin	-	+	+
4	Carbohydrates	+	+	-
5	Cardiac Glycosides	-	-	-
6	Coumarins		+	-
7	Flavonoids	++	+++	++
8	Glycosides	-	+	-
9	Phenols	-	++	-
10	Proteins	-	-	-
11	Quinones	-	+	-
12	Saponins	+	++	-
13	Starch	+	-	-
14	steroids	-	+	-
15	Tannins	++	+++	+
16	Terpenoids	+	+	+

Antioxidant Activity

As it is widely accepted that plants, herbs, spices rich in bioactive components and specifically flavonoids delay or prevent lipid peroxidation by scavenging free unpaired electrons which cause cellular and genetic changes affecting cell signaling systems and promotes senescence. Consumption of plants rich in bioactive components reduce oxidative damage and other oxidative stress related diseases (Gupta and Sharma, 2006). Thus, methanol extract of *I. verum* which revealed rich flavonoid content is analyzed for

Table 2 GC-MS spectrum of methanol extract of *Illicium verum*

No	Compounds Name	Retention Time (min.)	Molecular Formula	Molecular Weight	Cas	Norms %	Area %
1	Estragole	10.236	$C_{10}H_{12}O$	148	140-67-0	1.56	1.382
2	Benzene, 1-Methoxy-4- (1-Propenyl)-	11.477	$C_{10}H_{12}O$	148	140-67-0	6.05	5.353
3	1H-Indenol, 2,3-Dihydro-	11.972	$C_9H_{10}O$	134	36643-74-0	100.00	88.421
4	Bicyclo [3.1.1] Hept-2-Ene, 2,6-Dimethyl-6-(4-Methyl-3-Pentenyl)-	13.743	$C_{15}H_{24}$	204	17699-05-7	0.61	0.541
5	Benzeneacetic Acid, .Alpha.-Hydroxy-4-Methoxy	15.684	$C_9H_{10}O_4$	182	10502-44-0	0.93	0.821
6	Benzeneacetic Acid, .Alpha.-Hydroxy-2-Methoxy	15.764	$C_9H_{10}O_4$	182	10408-29-4	0.26	0.495
7	1-(3-Methyl-2-Butenoxy)-4-(1-Propenyl) Benzene	16.904	$C_9H_{10}O$	134	1470-94-6	3.38	2.988

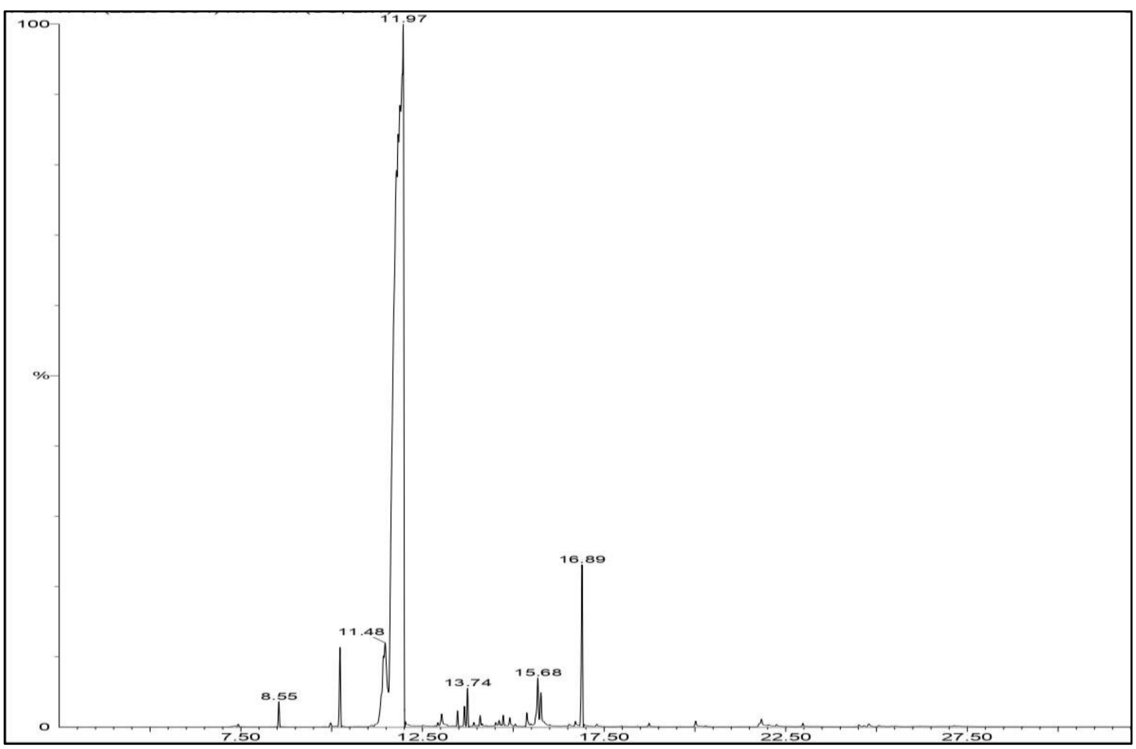
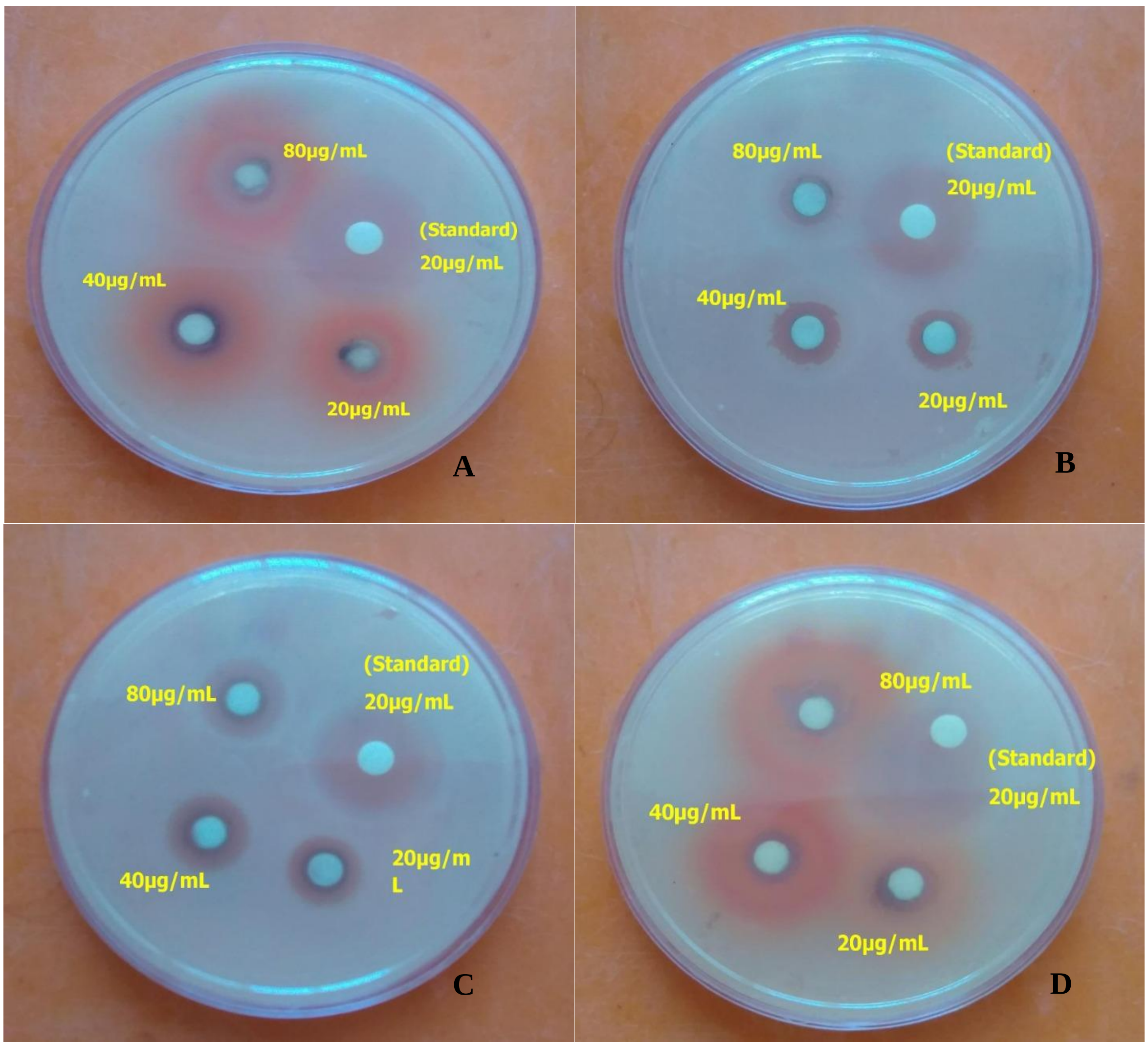


Figure 1 GC-MS spectrum of methanol extract of *Illicium verum*

antioxidant properties. Antioxidant activity of an extract can be estimated by IC_{50} value, lower the value higher the antioxidant property. Radical scavenging activity of various concentrations of Methanol extract of *I. verum* in comparison of L. Ascorbic acid as control revealed that at 20 (µg/ml) the scavenging activity which is expressed as IC_{50} value is 69.12±0.30 is almost equal to that of the Ascorbic acid value 75.3±0.25, used as standard. At the mid concentration, 40 (µg/ml) it is observed that a slight increase in antioxidant activity is 51.95±0.25 in comparison with that of the standard value 50.14±0.36. At the highest dosage of 80 µg/ml there is a significant increase in the antioxidant activity which is 26.95±0.35 and the standard value is 23.54±0.35. Fig 4 represents the mean values of triplicates for antioxidant activity.



A) *E. coli; B) K. pneumoniae*; C) *P. mirabilis*; D) *S. aureus*

Figure 2: Zone of inhibition by *I. verum* extract against drug resistant bacteria

DISCUSSION

Non judicious and continuous usage of many conventional, synthetic antibiotics against bacterial infections, has led to continuous evolution of multidrug resistance in them (Yu *et al.*, 2020) Bacteria like *S. aureus*, *P. aeruginosa*, *S. pneumoniae*, *A. baumannii*, *E. faecium*, *H. pylori Salmonellae* and *N. gonorrhoeae*, *Haemophilus influenzae*, and species of *Shigella* apart from their multi drug resistant property also exhibit a violent inbuilt feature of inheriting them through their genome influencing the other bacteria as well (Centers

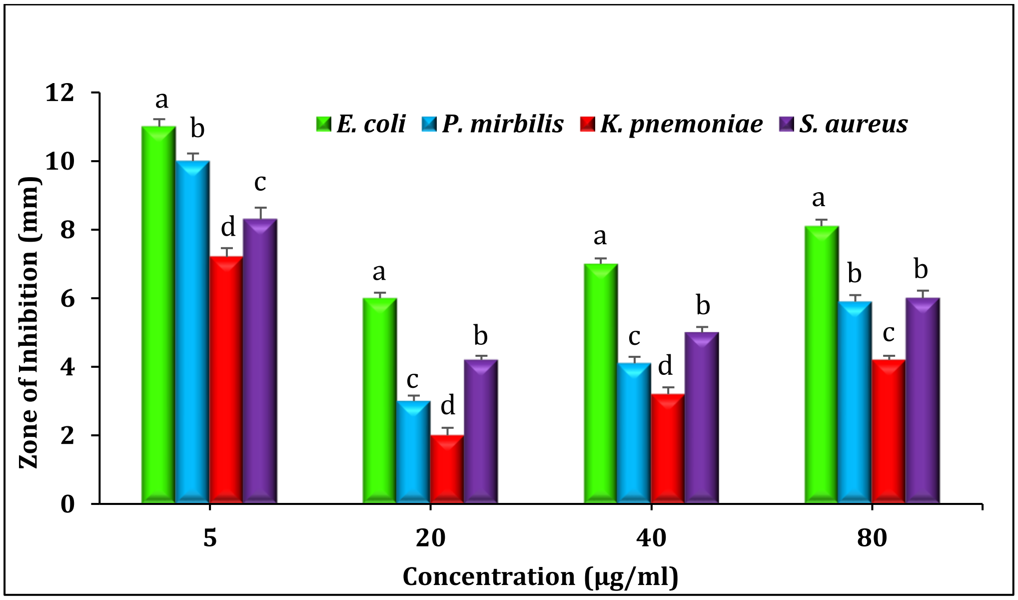


Figure 3: Antibacterial activity of methanol extract of *Illicium verum*. Values are expressed as mean ± SE of triplicates in each group.

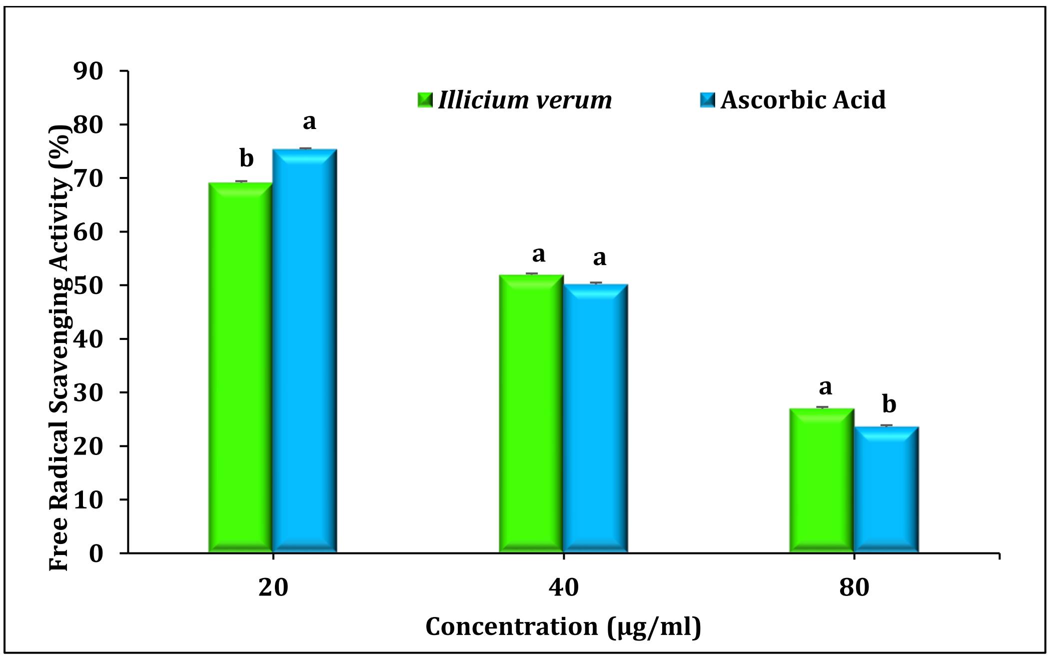


Figure 4: Evaluation of antioxidant activity efficacy of the methanol extract of *Illicium verum* by DPPH assay. Values are expressed as Mean ± SE of triplicates in each group

for Disease Control and Prevention, 2019) thus driving the healthcare system to search for new antibiotics to combat and reduce the death rate and morbidity in affected individuals. Contamination and pollution of various

habitats like large water bodies, soil, and air by drainage of hospital and industrial wastes, overuse of pesticides, release of harmful gasses by automobiles have paved a pathway for accumulation of antibiotic residue and other harmful chemicals associated with it in the food chain and fasten the emergence of antibiotic resistant pathogens in the community (Gothwal *et al.,* 2015; Said *et al.,* 2016; Oyekale *et al.,* 2017; Jonas *et al.,* 2017). It is reported that the drug resistance in bacteria could be achieved by interaction between the antibiotics and drug resistant determinants on the bacteria (Mak *et al.,* 2014; Munita *et al.,* 2016) enzymes produced by bacteria that an alter the chemical structures of antibiotics (Fischbach *et al.,* 2009), production of ß lactamase enzymes that could hydrolyse and disable the antibiotics such as penicillin and other advanced drugs like cephalosporin and monobactams are found to be linked with the conjugative plasmids (Rahman *et al.,* 2018), developing capacity to disturb the synthesis of protein at ribosome level (Wilson, 2014) reducing the antibiotic concentration inside the cell by throwing them out through permeability change of porins on cell membrane (Shriram *et al.,* 2018) structural change of antibiotic targets by methylation reduces the affinity between them and antibiotics thus developing resistance (Munita *et al.,* 2016). (Moellering, 2012) has reported that *S. aureus* has acquired a special kind of protein called penicillin binding proteins encoded by the mecA gene that developed methicillin resistance in them. Interestingly it is observed that transfer of genetic material both horizontally and intergenerational in bacteria have paved the way for adaptation against many antibiotics (Wiedenbeck *et al.,* 2011; Hall *et al.,* 2017; Saak *et al.,* 2020).Thus, the drying pipeline of efficient and nonhazardous antibiotics and urgency of adopting an alternate therapy has directed the pharma industry towards plant based therapeutic agents (Mbaveng *et al.,* 2015; Anand *et al.,* 2019; Anand *et al.,* 2020; Mohammed *et al.,* 2021) have reported that plants hold various bioactive molecules like phenols, tannins, alkaloids, coumarins, terpenes, terpenoids, flavonoids and various other potent components with medicinal properties. Herbs, spices and medicinal plants rich in phytochemicals in the form of powders and crude extracts have proven to be effective against illnesses like microbial infection, inflammation, fever, diabetes, cancer, lipid peroxidation etc. (Perumal Samy & Gopalkrishnakone, 2010; Dominguez-Perles *et al.,* 2020).
Supporting this report, our investigation on Chinese herb *I.verum* and results obtained on its phytochemical screening, GC-MS profile, antibacterial and DPPH activity have established that secondary metabolites of *I.verum* play an important role in its unique medicinal properties which can be explored to synthesize novel antibiotics to fight against various bacterial diseases and to be used as potential antioxidant. In the present study, among the three different solvent-based extracts of *I. verum*, viz. Diethyl ether, methanol and hexane, methanolic extract manifested a rich presence of bioactive molecules like flavonoids, tannins, phenol, saponins terpenoids etc. owing to its remarkable potency and solubility of phytochemical compounds (Table 1). (Reddy *et al.,* 2021) also reported a similar result in phytochemical screening of *Gardenia latifolia* using methanol extract due to its rich manifestation of secondary metabolites whereas hexane showed no compounds, chloroform showed the presence of phenols and flavonoids and ethyl acetate exhibited phenols, flavonoids, glycosides and terpenoids. Studies reveal that, in albino rats and mice, methanol extract of *I.verum* at the dose of 200 mg, reported a strong sleep inducing and anxiolytic behavior than hexane and ethyl acetate extracts, with no toxicity effects below 2000 mg and throw light on efficacy of *I.verum* in treating sleep disorders (Chouksey *et al.,* 2013). Studies reported by (Wei *et al.,* 2014) suggests that methanol extract of *I.verum* yields rich bioactive compounds compared to ethanol and petroleum ether indicating the influence of solvent characteristics and polarity of the phytocompounds and established that *I.verum* is rich in high polar components resulted in polarity values of methanol, ethanol and petroleum ether were 5.1, 4.4, and 0.0, respectively. Similar results were reported by (Vijayakumar *et al.,* 2012) that the yield percentage of methanol extract of both the seed and fruits of *I. griffithii* to be comparatively higher than the extracts of hexane and ethyl acetate. Absolute and 50% methanol extract of *I.verum* exhibited a remarkable efficacy as antiviral agents against reovirus in birds, virus causing avian nephrosis (IBDV), Conjunctivitis (NDV) and laryngotracheitis (ILTV) and exhibited toxic effects on cells against them (Alhajj *et al.,* 2020) Thus, within the references made and our promising results of phytochemical screening of the methanol extract of *I.verum* with the GC-MS study of the same conclude to a greater percentage that methanol could be a suitable solvent for extraction of high polar bioactive components of genus Illicium.

GC-MS study of methanol extract of *I.verum* in our investigation revealed the compounds like estragole, anethole, anisoles, terpenes and major percentage of phenolic compounds (Table 2 & Fig 1). (Patra *et al.,* 2020; Padmashree *et al.,* 2007; Yang *et al.,* 2021; Yang *et al.,* 2010) recorded the presence of bio active components like anisyl alcohol, anethole, anisyl acetone and anisyl aldehyde, within the SFE extracts of *I.verum* by GC-MS study. GC-MS analysis of methanolic extract of *I.verum* revealed anethole, m-methoxybenzaldehyde, and 3-Hydroxybutyric acid the prominent components and reported that these constituents are main reasons for inhibitory activity against biofilm forming *S. aureus* by docking studies (Ganesh *et al.,* 2022). Phytochemical characterization of silver nanoparticles *I.verum* by various other methods like UV-Vis, FTIR, XRD, SEM, TEM, AFM revealed bioactive components that exhibited antidiatom property (Lakhan *et al.,* 2020) elaborated the interactions of polyphenol residues with the Ag+ ions enhancing the antimicrobial property of anise seeds. Spectrophotometric studies of diethyl ether extraction of *I.verum* revealed (*E*)-anethole, anisyl alcohol, anisyl acetone and anisyl aldehyde with significant bactericidal effects on various clinical pathogens (Luna *et al.,* 2015).

Essential oil of *I.verum* encapsulated by **β** cyclodextrin as outer boundary wall has displayed a stronger antibacterial and antioxidative property ascertained by FTIR on encapsulation and ability to resist under heat stress by differential scanning calorimetry and thermogravimetric analysis (Wu *et al.,* 2022). TLC and HPTLC chromatogram studies of methanol extracts of *I.verum* potentiated a compound called phenobarbitone which can be used as sleep inducing natural substance in sleep disorders (Chouksey *et al., 2013). Various extraction methods of phytochemical analy*ses of *I.verum* have exposed the richness of tannins, phenols and flavonoids especially in methanol extract making it a promising candidate for antimicrobial and antioxidative properties.

In this investigation the highest dosage, 80 µg/ml of methanol extract of *I.verum* displayed a remarkable bactericidal effect against the chosen pathogens viz. *E.coli*, *K. pneumoniae*, *P. mirabilis* and *S. aureus* whereas the mid and the lower dose 40 µg/ml and 20 µg/ml also exhibited the inhibitory property but a slight decreasing trend was observed and a similar fashion of results were observed in antioxidative studies with a significant efficacy of 80 µg/ml of methanol extract revealing a low IC_{50} values almost close to the value of standard Ascorbic acid, whereas the other doses also revealed a positive result but comparatively milder, as reported by (Agbor *et al.,* 2014) that hydroxyl radical scavenging activities have increased in a concentration-dependent manner. Our results also establish a very strong positive correlation between the richness of flavonoids and phenolic compounds and antibacterial activity, eventually antioxidant properties supporting the previous work of (Cai *et al.,* 2004; Shan *et al.,* 2005) in dietary spices and Chinese herbs and by (Bobinaite *et al.,* 2020; Magharbeh *et al.,* 2020) in plant extracts.(Del Rio *et al.,* 2013; Miklasinska-Majdanik *et al.,* 2018; Zacchino *et al.,* 2017; Lima *et al.,* 2019; Makarewicz *et al.,* 2021) report that phytophenols can suppress the antibiotic resistance in bacteria eventually either killing or arresting their proliferation thus acting as natural antibiotics. Dietary and medicinal herbs inclusive of *I.verum* exhibit a remarkable antibacterial activity against food pathogens (Shan *et al.,* 2007). Further our thorough references reveal similar reports from other plant sources like essential oils of thyme, clove, cinnamon, oregano (Karapinar *et al.,* 1987; Beuchat *et al.,* 1989) ellagitannin of pomegranate (Negi *et al.,* 2003; Voravuthikunchai *et al.,* 2004; Voravuthikunchai *et al.,* 2005; Machado *et al.,* 2002). Studies show that extracts of citronella, neem, oregano, aloevera, evergreen shrub rosemary, aromatic herb thyme, tulsi and bryophyllum exhibit remarkable inhibitory effects on methicillin resistant $Gram^+$ and $Gram^-$ bacteria and ascertained the role of tannins and phenols against them (Dahiya *et al.,* 2012). Similar to our study, in vitro studies of turmeric, ginger and *Tinospora* against clinical pathogens like *S. aureus, P. aeruginosa, K. pneumoniae, E. coli, B. subtilis* and *P. mirabilis* found to exhibit an effective bactericidal action (Chakraborty *et al.,* 2014). Plant phenols including pyrogallol and catechol (Shahzad *et al.,* 2015; Liu *et al.,* 2021; Taguri *et al.,* 2006) mushrooms rich in hydroxycinnamic acid derivatives and other phenolic acids exhibit significant antimicrobial effects (Nowacka *et al.,* 2015). Caffeic acid, a polyphenol present in the leaf extract of olives, could interact with the domains of ampicillin resistance in *S. aureus* and *E. coli* facilitating the bactericidal effect on them (Lim *et al.,* 2016). Studies reveal that flavonoids and their derivatives of plants exhibit efflux mechanism of promoting the antibiotics to act on the resistant property of *S. aureus* thus establishing the antimicrobial property (Chan *et al.,* 2011; Randhawa *et al.,* 2016; Klancnik *et al.,* 2017; Christena *et al.,* 2015; Lopes *et al.,* 2017; Gorniak *et al.,* 2019; Xu *et al.,* 2019) changes the structural orientation of cell membrane (Cushnie *et al*, 2008) alters the membrane integrity (Budzynska *et al.*, 2011) in methicillin resistant *S. aureus* and *E. faecalis*. (Wu *et al.*, 2013) have reported that there is strong interaction between the flavonoids and the gyrase enzyme thus inhibiting the replication of bacterial DNA and (Lin *et al.*, 2005) has reported about the behavior of flavonoids against antibiotic resistant strains of *K. pneumoniae* and ascertained the capacity of flavonoid as resistant reversal agents.

It appears that the presence of terpenes in our crude methanol extract of *I. verum* fruit also owes to its bactericidal property. Understanding the relationship and mode of action between the bioactive components and pathogenic bacteria, many researchers have studied and reported that presence of terpenes in the extracts of essential oil of *I. verum* exhibited a significant antibacterial property against *S. aureus* amongst six other bacteria with MIC of about 1/1000 (v/v) and antioxidant activity with IC_{50}= 286.19 ± 7.4 mg/ml, compared to Ascorbic acid IC_{50}= 0.09 ± 0.01 mg/ml (Outemsaa *et al.*, 2021) antibacterial activity against *A. baumannii* (Luis *et al.*, 2019) against *E. coli, B. cereus, S. typhi and S. aureus* than water extract (Sabry *et al.*, 2021; Li *et al.*, 2021) also against *S. pyogenes* and *P. aeruginosa* (Li *et al.*, 2021). (Yu *et al.*, 2020) has listed that EOs display their potentials against drug-resistance by various mechanism as mentioned by (Fischbach *et al.*, 2009; Mak *et al.*, 2014; Munita *et al.*, 2016; Rahman *et al.*, 2018; Wilson, 2014; Pages *et al.*, 2008; Shriram *et al.*, 2018; Moellering, 2012) essential oil like thymol and carvacrol in *Thymus Capitatus* against *P. aeruginosa* (Althunibat *et al.*, 2016) eugenol against methicillin resistant *S. aureus* (Yadav *et al.*, 2015; Togashi *et al.*, 2010; Muniz *et al.*, 2021). Cinnamon EOs against *E. coli* and Staphylococcus strains (Zhang et al., 2015) *Coriandrum sativum* EOs against uropathogenic *E. coli* (Scazzocchio *et al.*, 2017) could disrupt the cell membrane changing its integrity and bring out a bactericidal effect. Presence of coumarins in our phytochemical screening suggests both the antibacterial and antioxidant characteristics of *I. verum* (Basile *et al.*, 2009; Tan *et al.*, 2017; El-Seedi *et al.*, 2007) have reported that coumarins act on the MDR bacteria as DNA gyrase inhibitor thus arresting the replication bacterial DNA and act as resistance reversal agents. (Bazzaz *et al.*, 2010) says that coumarins could also behave as an inhibitor of efflux mechanism against *S. aureus.* Evidently the presence of saponins in our screening could also account for the antibacterial activity exhibited by *I. verum.* Amphiphilic properties of saponins promote formation of foams that could be bactericidal in aqueous solutions (Vincken *et al.*, 2007; Moghimipour *et al.*, 2015) play a very important role as an antimicrobial agent (Sparg *et al.*, 2005; Sengul *et al.*, 2011; Veda *et al.*, 2017; Mert Eren *et al.*, 2021). (Charalambous *et al.*, 2022) reported about nine saponins and six phenolic compounds responsible for the bactericidal effect of root extract of *Saponaria cypria Boiss*. Similarly, saponin-enriched *Catharanthus roseus* root extract also exhibited the antioxidant, anti-proliferative and antibacterial effect against *E. coli*, *E. aerogenes* and *S. lugdunensis*, antifungal properties against *Candida albicans* and *Aspergillus niger* (Pham *et al.,* 2019). Methanol extract of *I. verum* revealed rich tannins which are main components of Chinese medications well known for their antimicrobial behavior acting as protein binders and precipitating them. (Zhang *et al.*, 2012) has reported the role of tannins as antiviral agents in 50 Chinese herbs. Plant extracts rich in tannins display a remarkable antibacterial activity against *S. typhi* in *Euphorbia hirta* (Perumal *et al.*, 2012) acetone and water extracts of *Terminalia arjuna a*nd *Piper betel* against *B. subtilis, S. aureus, E. faecalis, M. luteus* ($Gram^+$) and *E. coli, K. pneumoniae, S. typhi,, P. aeruginosa, P. vulgaris*,($Gram^-$), (Kurhekar, 2016) leaves extract of *Arum maculatum* against (*S. aureus and L. monocytogenes*) and $Gram^-$ bacteria (*E. coli, S. enteritidis,* and *P. aeruginosa)* (Farahmandfar *et al.*, 2019) antifungal property against Candida albicans and *Aspergillus niger* (Banso *et al.*, 2007).

Establishing through our GC-MS study of methanol extract of *I.verum* which revealed a majority of phenolic compounds like benzoic acid derivatives and flavonoids, it is evident that apart from its antimicrobial action it also exhibits a significant property of scavenging free oxygen radicals. WHO has recommended that at least a dietary intake of 400g of fruits and vegetables rich in antioxidants (Jurikova *et al.*, 2017) is important for protecting against chronic diseases (Mendoza *et al.*, 2018) and cardiovascular diseases (Hartley *et al.*, 2013; Griffiths *et al.*, 2016). Researchers say that antioxidant rich food supplements act as dietary intervention therapy against neural aging, microglia senescence and other neurodegenerative diseases (Wu *et al.*, 2016; Franco *et al.*, 2017; Bouarab-Chibane *et al.*, 2019) Natural antioxidants are found in plants, microorganisms, fungi, and even animal tissues (Charles, 2012). and they are primarily phenols, flavonoids, cinnamic acids, hydroxybenzoic acids and curcuminoids (Zeb, 2021). Phenolic antioxidants in plants are involved in complex metabolic and signaling mechanisms and protect plants against invasion of microbes by producing phytoalexins, a flavonoid derivative (Ahuja *et al.,* 2012). Natural antioxidants like flavonoids, coumarins, tocopherols, polyphenols from plant materials primarily acts as reducing agents, free oxygen radical scavengers and could suppress the formation of oxygen singlets (Pratt, 1992). It is also supported that spices and herbs can slow down the lipid oxidation because of their remarkable antioxidant property, improving preservation and prolonged shelf life of foods (Yu *et al.*, 2021; Emboscado, 2015; Rutkowska *et al.*, 2020; Kozlowska *et al.,* 2014; Kozłowska *et al.,* 2019). Herbs and spices rich in antioxidants can scavenge the free radicals in the early stages of auto oxidation with their ability of forming complexes with the metal ions (Wang *et al.,* 2021) remarkably reduces the oxidative damage of foods (Estevez *et al.,* 2017). (Wang *et al.,* 2021) has reported that micro-encapsulated poly phenols of *I.verum* show an exceptional antioxidant activity. Methanolic extract of Star anise significantly reduces oxidative stress by arresting the enzyme catalase and glutathione-peroxidase activity in murine models (Majali, 2022). Also reported that the methanolic extract of *I.verum* rich in protocatechuic acid (Bhatti *et al.,* 2017) ethyl acetate fractions with phenolic acid like gallic acid and flavonoids, quercetin (Yang *et al*., 2012), Aqueous extract rich in polyphenols (Dinesha *et al.*, 2012), essential oil of *I.verum* rich phenylpropanoids including trans-anethole (Outemsaa *et al.*, 2021) shikimic and anisic acid exhibited antioxidant activity (Li *et al.,* 2021). Presence of Flavonoids in our methanol extract establishes a probable reason for antioxidant activity of *I.verum* as explained by (Hes *et al.*, 2019) that cyclooxygenase and lipoxygenase enzymes that cause oxidative damage in foods are hampered by flavonoids in Aloe vera.

Lipid oxidation spoils the food, changing the taste, odor, texture leading to oxidative deterioration, damaging the nutritive value interlinked with the microbial spoilage have driven us to overuse of preservatives and led to over usage of synthetic antioxidants (Eshghi *et al.,* 2014; Farahmandfar *et al.,* 2015; Prakash *et al.,* 2020) dangerous to human health (Gupta and Sharma, 2006). It is suggested that herbs and spices rich in phytochemicals to be used as a substitute for man-made antioxidants in foods (Shan *et al.*, 2005; Srinivasan, 2014; Asnaashari *et al.,* 2015) and complete source through food (Farahmandfar *et al.*, 2015; Paur et al., 2011), improving the wellness (Yashin *et al.*, 2017; Huang, 2018), biofactors in fermented grains reduce the fatty acid oxidation (Morita *et al.,* 2018) medicinal plants rich in Selenium accumulation act as very efficient antioxidants (Golubkina *et al.,* 2020). Rosemary ginger, curcuma, black pepper, red pepper, chili, pepper, marjoram, and Licorice are the most promising antioxidants found in spices and herbs (Khanam *et al.,* 2021). Different extracts of *Laurus nobilis. L* leaves rich in quercetin as potential antioxidants ascertained by various free radical scavenging assays, are used to treat rheumatism and skin diseases (Kaurinovic *et al.*, 2019). Thus, concluding with our study and references, the richness of trans-anethole in *I.verum* fruit proved to be an excellent bioactive component responsible for many of its therapeutic properties. It is established that the antibiotic mupirocin mixed with trans-anethole exhibited an increased antibacterial activity against *S. aureus* (Kwiatkowski *et al.*, 2019) trans-anethole on quorum sensing exhibit bactericidal action against *E. coli* (Hancer *et al.,* 2018). Docking studies have ascertained that limonene, estragole and trans anethole play a very important role in both the antibacterial and antioxidant activity of *I. verum* (El-Kersh *et al.,* 2022) and the same in our GC-MS analysis enlightening that the methanol extract *I. verum* with all the bioactive molecules open a new avenue of adapting fruits of *I. verum* as a novel antimicrobial and antioxidant agent to meet the demands of current scenario of alternative therapeutic agents.

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