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# IDENTIFICATION OF BIOACTIVE MOLECULES AND MOLECULAR DOCKING STUDIES OF TURMERONE FROM *Curcuma longa* ROOT EXTRACT

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## ABSTRACT

The investigation of bioactive molecules and molecular docking studies of *Curcuma longa* roots extract was conducted using various techniques, cold extraction method was used to obtain the extract from the *Curcuma longa* roots, Phytochemical Screening allowed the identification of various phytochemicals in the *Curcuma longa* roots extract, such as alkaloids, tannins, flavonoids, steroids and glycosides, GC-MS analysis of *Curcuma longa* root extract revealed the presence of twenty-two chemical compounds, five (5) compounds ( Tumerone, Caryophyllene oxide, Stigmasterol, Gamma-sitosterol, Cholest-4-en-3-one) were identified as the most active providing information on the individual compounds present. Molecular docking studies shows the potential binding energies and modes of action (-6.8 against 4PQE and -7.5 against 1XV8). of the chosen bioactive molecule in the extract. The results of these studies have shown that turmerone could exhibits significant antibacterial activity against the strains of bacteria.

**Keywords:** Bioactive molecules, *Curcuma longa*, Molecular docking, turmerone.

## INTRODUCTION

*Curcuma longa* is a plant that has a very long history of medicinal use, dating back nearly 4000 years. In Southeast Asia, *Curcuma longa* is used not only as a principal spice but also as a component in religious ceremonies. Because of its brilliant yellow color, *Curcuma longa* is also known as "Indian saffron. *Curcuma longa* is used as an herbal medicine for rheumatoid arthritis, chronic anterior uveitis, conjunctivitis, skin cancer, small pox, chicken pox, wound healing, urinary tract infections, and liver ailments (Zeng *et al*., 2022). It is also used for digestive disorders; to reduce flatus, jaundice, menstrual difficulties, and colic; for abdominal pain and distension (Fuloria *et al*., 2022)); and for dyspeptic conditions including loss of appetite, postprandial feelings of fullness, and liver and gallbladder complaints. It has anti-inflammatory, choleretic, antimicrobial, and carminative actions (Mdills and Bone 2000). The main clinical targets of *Curcuma longa* are the digestive organs: in the intestine, for treatment of diseases such as familial adenomatous polyposis (Cruz-Correa *et al*. 2006); in the bowels, for treatment of inflammatory bowel disease (Hanai and Sugimoto 2009); and in the colon, for treatment of colon cancer (Naganuma *et al*., 2006). Helicobacter pylori gastritis causes a mixed acute and chronic

inflammatory reaction, stimulating both neutrophils and eosinophils, as well as mast and dendritic cells. *Curcuma longa*, a perennial herb from the Zingiberaceae family, has a long history of traditional medicinal use and is widely recognized for its diverse biological activities. The bioactive compounds present in *Curcuma longa* roots, especially the phenolic compounds known as curcuminoids, have attracted considerable attention due to their potential antimicrobial, anti-inflammatory, antioxidant, and anticancer properties. Curcuminoids, including curcumin, demethoxycurcumin, and bisdemethoxycurcumin, are considered the primary bioactive constituents in *Curcuma longa* roots. These compounds have been extensively studied for their antimicrobial activities against various pathogens, including bacteria, viruses, and fungi. Their mechanisms of action involve targeting bacterial cell membranes, inhibiting enzymes crucial for bacterial survival, and interfering with bacterial adhesion to host cells (Yang *et al*., 2020).

## Experimental Procedure

### Plant Material

*Curcuma longa* root, was collected and air dried in August 2023, from Ugbomro, Delta, Nigeria. The plant was authenticated by botanists in the Department of Biological Science, Faculty of life sciences, Federal University of Dutsin-ma, Nigeria.

### Collection of Plant, Extraction and Isolation Method of the Compound

*Curcuma longa* root was collected, air-dried, grounded (300g), macerated with ethanol and concentrated using rotary evaporator to give 7.0g.

### Preliminary Phytochemical Screening:

The crude extract of ethanol was subjected to preliminary qualitative screening of secondary metabolites using standard methods of Evans (2002), Silva *et al*. (1998) and Sofowora (1996).

## Results and Discussion

**Table 1: Qualitatve Phytochemical Analysis of the Extract**

| Test Compounds | Ethanol Extract |
|---|---|
| Saponins | + |
| Flavonoids | + |
| Alkaloids | + |
| Phenolics | + |
| Tannins | - |
| Anthraquinones | - |
| Terpenes | + |
| Steroids | + |

Key: +=present,-= Absent

The qualitatve phytochemical analysis of the extract revealed the presence of steroid, terpenes saponins, flavonoids, alkaloids, phenolics,whereas tannins and anthraquinones were absent (Table 1). The presence of these compounds from the root of the plant could be the linked to the ethnomedicinal uses of the of *Curcuma longa* in traditional medicine practices.

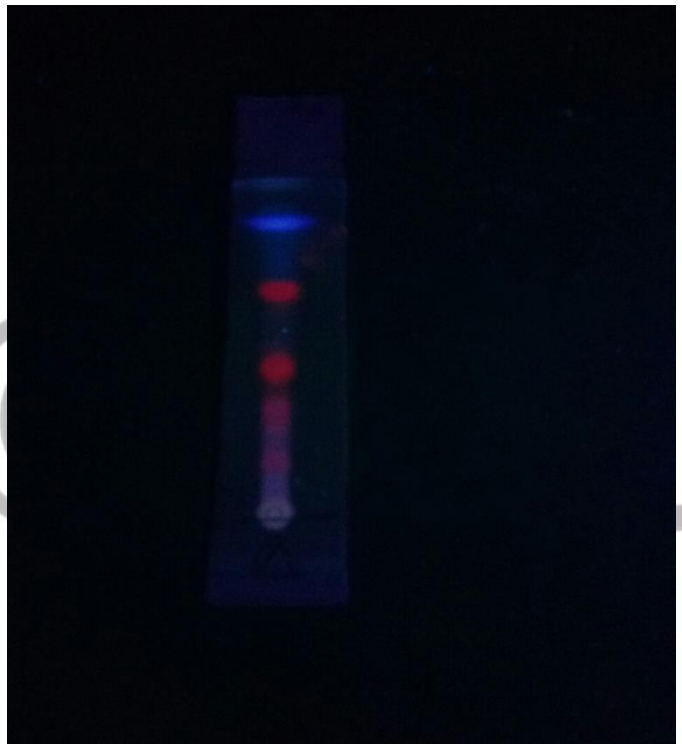


**Fig. 1 TLC Profile of the crude extract**

**Table 2: $R_f$ values of the component**

| Components | Distance travelled by the compound | Distance travelled by the solvent system | Retention factor |
|---|---|---|---|
| E1 | 0.70 | 5.50 | 0.12 |
| E2 | 1.40 | 5.50 | 0.25 |
| E3 | 2.20 | 5.50 | 0.40 |
| E4 | 3.50 | 5.50 | 0.64 |
| E5 | 4.00 | 5.50 | 0.72 |

The root extract of *Curcuma longa* was subjected to thin layer chromatography (TLC) using solvents system (Hexane per ethyl acetate (4.5:0.5), the extract was then spotted on TLC plate and then developed by dipping the end below the spot in a solvent system; the plate and the container being kept in a closed airtight. The TLC chromatograph was viewed using UV of 364nm. The compounds on the TLC sheet showed different color at different region with $R_f$ values ranged (0. 1- 0.72).

**G-C Chromatogram of *Curcuma longa***

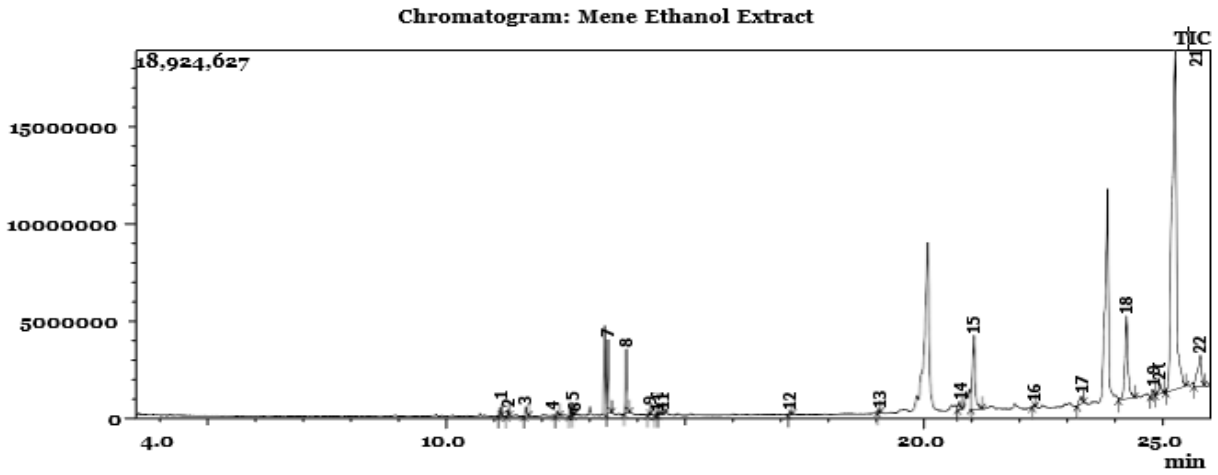



**Fig. 2 G-C Chromatogram of the root extract of *Curcuma longa***

GC-MS analysis of Ethanol extract of *Curcuma longa* rhizomes from revealed the presence of twenty two chemical compounds, namely: Benzene, 1-(1,5-dimethyl-4-hex), 1,3Cyclohexadiene, 5-(1,5-dim), Cyclohexene, 3-(1,5-dimethyl-4), Benzene, 1,1'-(1,1,2,2-tetrameth), Benzene, 1,4-dimethyl-2-(2-me), Caryophyllene oxide, Turmerone 4,2,8-Ethanylylidene-2H-1-ben, Naphthalene, 1,1'-(1,10-decaned), Turmerone, Benzene, 1,1'-(1,1,2,2-tetrameth), Hexadecenoic acid, ethyl ester, Ethyl Oleate, Tetrapentacontane, 1-Hexacosanol, Oxirane, hexadecyl-, Octacosanol, Stigmasterol, 16-Hentriacontanone, Stigmasterol, gamma.-Sitosterol, Cholest-4-en-3-one. From the result, Naphthalene, 1,1'-(1,10-decaned), was the least abundant (1.65) and gamma-Sitosterol was more abundant (6.65). from the twenty-two (22) chemical compounds. In addition, five (5) bioactive compounds were identified from the known chemical compounds present. The bioactive compounds are Caryophyllene oxide (Woo *et al*., 2020), Tumerone

(Iweala *et al*., 2023), Octacosanol, Stigmasterol, Gamma-sitosterol, Cholest-4-en-3-one (Junichi *et al*., 2021).

**Structures of the five major Compounds Identified from the G-C Analysis of *Curcuma longa* root extracts**

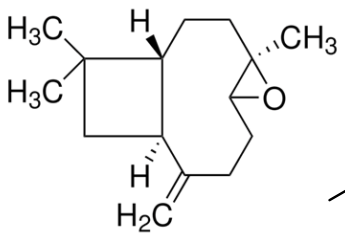



**Fig: 3. Caryophyllene Oxide**

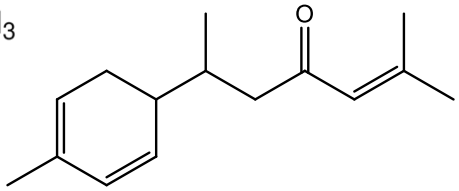
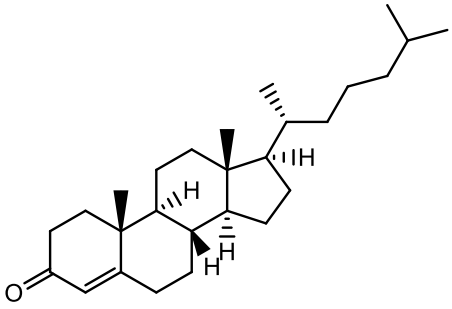



**Fig: 4. Turmerone**




**Fig; 5. Cholest-4-en-3-one**

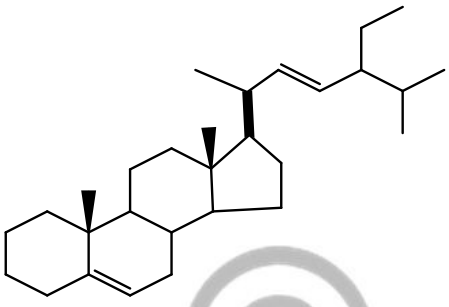


**Fig: 6. Stigmasterol**

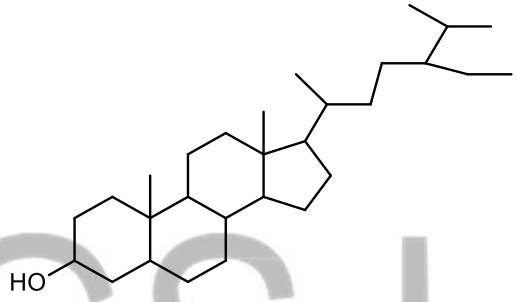



**Fig: 7. Gamma-sitosterol**



**Pharmacological Potentials of the five Major Bioactive Compounds Identified**

A randomized double-blind, placebo-controlled study investigated the inhibitory effects of β-caryophyllene on H. pylori and its potential role as an alternative gastrointestinal drug. The study found that β-caryophyllene could be a promising candidate for H. pylori eradication (Shim *et al*., 2019). β-caryophyllene has been shown to possess inhibitory activity against the expressions of replication genes of H. pylori, such as CagA, VacA, SecA, T4SS, dnaE, and dnaN (Woo *et al*., 2020) A study investigated the effects of β-caryophyllene from cloves extract on H. pylori eradication in a mouse model and its effects on gastric mucosa inflammation (Jung *et al*., 2020). Cholest-4-en-3-one (cholestenone) has been found to exhibit antibacterial activity against Helicobacter pylori by inhibiting the biosynthesis of the cell wall component CGL (cholesteryl-α-D-glucopyranoside. Cholest-4-en-3-one" refers to a specific chemical compound, which is a ketone derivative of cholesterol (Hucklenbroich *et al*., 2014). Stigmasterol, an unsaturated phytosterol found in various plants, possesses antimicrobial properties that can fight against bacteria. Research has shown that stigmasterol exhibits bacteriostatic and bactericidal activities against various bacteria. Stigmasterol has also demonstrated antifungal properties. These findings suggest that stigmasterol holds promise as a natural compound with potential antibacterial and antifungal effects (Eftekhari *et al*.,2021). Research was conducted on the potential anti-cancer properties of gamma-sitosterol, suggested that it may inhibit the growth of certain cancer cells and induce

apoptosis, though more research is needed to establish its efficacy and safety in this regard (Sundarraj *et al*., 2012).

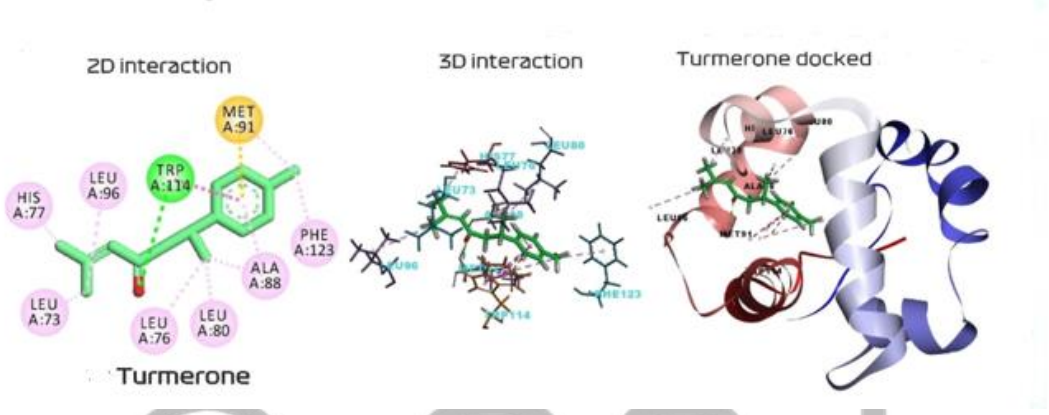
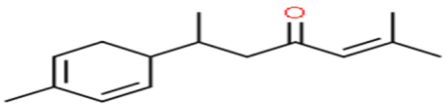



**Fig. 8 Molecular Docking**



**Table 3 Molecular Docking**

| Compound | Molecular Structure | Descriptor | Value |
|---|---|---|---|
| Turmerone |  | Molecular weight<br>LogP<br>Rotatable bonds<br>Acceptors<br>Donors<br>Surface area | 216.567<br>4.05677<br>4<br>1<br>0<br>98.677 |

Turmerone, a principal phytoconstituent found in *Curcuma longa*, functions as a human anticholinesterase (AChE) inhibitor (4PQE). The investigation demonstrates that the compound Ar-Tume, which was chosen, exhibited notable biological docking scores and negative binding energies (-6.8 against 4PQE and -7.5 against 1XV8).

## Conclusion

The qualitative analysis of the extract indicated the presence of steroid, terpenes saponins, flavonoids, alkaloids, and phenolics, while tannins and anthraquinones were found to be absent. Utilizing a solvent system of Hexane/ethyl acetate (4.5:0.5), the root extract of *Curcuma longa*

underwent thin layer chromatography (TLC), revealing compounds on the TLC sheet with varying colors at different regions and Rf values ranging from 0.1 to 0.72. An examination through GC-MS of the Ethanol extract of *Curcuma longa* identified twenty-two chemical compounds, with five bioactive compounds distinguished among the known chemical components. Turmerone, a key phytoconstituent within *Curcuma longa*, acts as a human anticholinesterase (AChE) inhibitor (4PQE). The study showcases that the selected compound Ar-Tume displayed significant biological docking scores and negative binding energies (-6.8 against 4PQE and -7.5 against 1XV8).

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