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ZINGIBER OFFICINALE EXTRACT: ANTIMICROBIAL PROPERTIES PHYTOCHEMICAL SCREENING, DRUG LIKENESS AND PHYSICOCHEMICAL STUDIES

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ABSTRACT

The extract of Zingiber officinale rhizomes commonly known as ginger was obtained utilizing soxhlet extraction assembly with methanol and n-hexane as solvents. Both parts (methanol and n-hexanes) were subjected for antimicrobial screening employing disc diffusion method against *S. aureus, S. epidermidis, P. mirabilis* and *E. Coli* bacteria. Findings for antimicrobial activity portrayed that the methanol extract of ginger has more advantage over the hexane extract. The literature described that ginger extract is composed of gingerol, zingiberene, β-bisabolene, α-farnesene, shogaol, β-sesquiphellandrene and α-curcumene. The computational studies such as calculation of drug likeness and physicochemical properties were performed for all the components. The computational results showed that all the components have good bioactivity score except component-7, and out of all components, the component-2, 3, 4 and 7 were found against the Lipinski rule of five with respect to the partition coefficient. Molecular docking studies were carried out to support the experimental results which states that hydrogen bonding with the receptor is found only in case of gingerol and shogaol and both the components were found mainly in methanol extract.

KEYWORDS Ginger extract, antimicrobial activity, drug likeness, physicochemical and molecular docking studies.

INTRODUCTION

The development of resistance because of multidrug-resistant bacteria and fungi to the presently available antimicrobials is of great concern to health care.[1] The incomplete course of antibiotics, mutation and genetic exchange system conducted the antimicrobial resistance.[2] The methicillin-resistant Staphylococcus aureus (MRSA) exhibited resistance to methicillin, cephalosporins, all beta lactams, gentamicin, erythromycin and trimethoprim/sulfamethoxazole while vancomycin-resistant enterococcus (VRE), represented resistant to vancomycin, ampicillin, and gentamicin.[3] Besides these many other organisms also developed resistance to the antimicrobials.[4] The pharmacological investigation of plant extract and plant derived compounds has been broadly studied and important globally affecting both world and international trade.[5-10] The traditional medicinal plants contributed as a centre for healthcare system for a big population.[5-10] Ginger (Zingiber officinale), a representative of the Zingiberaceae family, is everyday spice in many Asian countries.[11] It has been found to possess enormous pharmacological applications such as anticancer, anti-inflammatory, antimicrobial, fever, common cold, diabeties, antioxidant, anti-lipid, analgesic, antipyretic, anti-tumor, immunomodulatory effects, antiviral, rheumatic and gastrointestinal disorders.[12-25] It has also been found to cure nausea by chemotherapy, sea and morning sickness.[26] The ginger rhizomes comprises of the components are as follows gingerol, zingiberene, β-bisabolene, α-farnesene, shogaol, β-sesquiphellandrene and α-curcumene, out of all gingerol and shogaol were found in majority.[27, 33] The ginger extract has been broadly evaluated against a lot of bacteria and fungi.[28-33] The versatile pharmacological importance of ginger prompting us to study the antimicrobial activity of ginger extract, its composition, drug likeness and physicochemical properties, so that it can be used as lead finding for antimicrobial agent.

Experimental

Extraction

The extraction of the compounds from Zingiber officinale was produced on employment of Soxhlet extraction assembly, methanol and n-hexane solvent. The ginger rhizomes were grounded and kept inside a thimble loaded into the soxhlet extractor for 15 hr in the solvent (300 mL) with refluxing at the boiling temperature of

solvent. After completion of extraction the solvent was evaporated by vacumm rotary evaporator (Heidolph laborata/Germany).[27,33] The obtained extract was incubated at 40^0C for 24 hr, after that stored at 4^0C evaluation for antimicrobial activity.

Antimicrobial activity

Organism culture and *in vitro* screening for antibacterial activity was done by the same procedure reported in our previous articles.[34-40] *S. aureus, S. epidermidis, P. mirabilis* and *E. coli* were subcultured in Nutrient Agar medium and incubated for 18 h at 37 °C. Following the incubation the bacterial cells were suspended, according to the McFarland protocol in saline solution to produce a suspension of about 10^5 CFU/mL. 10 mL of this suspension was mixed with 10 mL of sterile antibiotic agar at 40 °C and poured on to an agar plate in a laminar flow cabinet. Five paper disks (6.0 mm diameter) were fixed onto nutrient agar plate. One milligram of each extract was dissolved in 100 ml methanol/n-hexane to prepare stock solution. From the stock solution different dilutions of each test portions were prepared and poured over disk plate. Ciprofloxacin was used as a standard drug (positive control), methanol and hexane as negative control. The susceptibility of the bacteria to the test compounds was determined by the formation of an inhibitory zone after 18 h of incubation at 36 °C.

Physicochemical properties[41-48]

The drug likeness score was calculated by considering partition coefficient (log P), molar refractivity, molecular weight, number of heavy atoms, number of hydrogen donor, number of hydrogen acceptor and number of violation by the software available online at www. molinspiration.com.

Bioactivity score[41-48]

The components were also checked for the drug likeness by calculating the bioactivity score for GPCR ligand, ion channel modulator, kinase inhibitor, nuclear receptor ligand utilizing online available software (www. molinspiration.com).

RESULT AND DISCUSSION

Antimicrobial activity

Antibacterial activity was performed by the disk diffusion method with minor modifications. *S. aureus, S. epidermidis, P. mirabilis* and *E. coli* were subcultured in Nutrient Agar medium using ciprofloxacin was used as a standard drug, methanol and hexane as negative control. The susceptibility of the bacteria to the test portion was determined by the formation of an inhibitory zone after 18 h of incubation at 36 °C. **Table-1,2 and 3** shows the zone of inhibition of the methanol extract, hexane extract and ciprofloxacin**.**

The phytochemical screening

The phytochemical screening indicated the presence of the components gingerol, zingiberene, β-bisabolene, α-farnesene, shogaol, β-sesquiphellandrene and α-curcumene.[27, 33]

Physicochemical properties[41-48]

Lipinski's rule of five states that, in general, an orally active drug has not more than 5 hydrogen bond donors (OH and NH groups), not more than 10 hydrogen bond acceptors (notably N and O), molecular weight under 500 g/mol, partition coefficient log P less than 5, number of violation less than 4. Only the components one, five and six were found completely in compliance with the Lipinski's rule, rests are deviated because of the greater partition coefficient, tabled in Table-4.

Bioactivity score.[41-48]

The bioactivity score was calculated for GPCR ligand, ion channel modulator, kinase inhibitor, nuclear receptor ligand, protease inhibitor and enzyme inhibitor. For average organic molecule the probability of bioactivity score is more than 0.00 then it is active, −0.50 to 0.0 then moderately active and if less than −0.50 then inactive. The results for bioactivity score are presented in Table 5. All the components showed the good bioactivity score except component-7.

Table: 1. Representing zone of inhibition for methanol extract of Zingiber Officinale against gram positive and gram negative bacteria.

Extract (µg/ml)	Effect of methanol extract on Microorganism			
	Gram positive		Gram negative	
	S. aureus	***S. epidermidis***	***P. mirabilis***	***E. coli***
50	19.12±0.10	18.78±0.22	13.12±0.24	18.44±0.10
25	14.32±0.08	13.08±0.14	10.42±0.32	14.14±0.16
12.5	09.06±0.52	07.14±0.40	-	10.32±0.30
6.25	-	-	-	08.14±0.32
3.125	-	-	-	-

Table: 2. Representing zone of inhibition for n-hexane extract of Zingiber Officinale against gram positive and gram negative bacteria.

Extract (µg/ml)	Effect of n-Hexane extract on Microorganism			
	Gram positive		Gram negative	
	S. aureus	*S. epidermidis*	*P. mirabilis*	*E. coli*
50	15.14±0.22	14.42±0.34	11.12±0.34	14.14±0.16
25	11.22±0.24	8.12±0.22	-	09.54±0.32
12.5	-	-	-	-
6.25	-	-	-	-
3.125	-	-	-	-

Table: 3. Representing zone of inhibition for ciprofloxacin, methanol and hexane against gram positive and gram negative bacteria.

Microorganism			
	Ciprofloxacin (10 µg/ml)	Methanol	Hexane
S. aureus	21.46 ±.31	-	-
S. epidermidis	22.64±.54	-	-
P. mirabilis	22.24±.30	-	-
E. coli	23.82±.47	-	-

Table-4: Representing the physicochemical properties of all the components found and ciprofloxacin.

Physicochemical property score	Components							
	1	2	3	4	5	6	7	Standard
miLogP	3.22	5.12	5.46	5.82	4.35	4.90	5.82	-0.701
TPSA	66.76	0.00	0.00	0.00	46.53	0.00	0.00	74.569
Natoms	21	15	15	15	20	15	15	24.0
MW	294.39	204.36	204.36	204.36	276.38	204.36	202.34	331.347
nON	4	0	0	0	3	0	0	6
nOHNH	2	0	0	0	1	0	0	2
Nviolations	0	1	1	1	0	0	1	0
Nrotb	10	4	4	6	9	4	4	3
Volume	295.61	234.35	234.88	239.27	281.38	234.90	228.14	285.46

Table-5: Representing the bioactivity score of all the components found in and ciprofloxacin.

Bioactivity score	Components							
	1	2	3	4	5	6	7	Standard
GPCR ligand	0.16	-0.39	-0.32	-0.30	0.06	-0.38	-0.47	0.12
Ion channel modulator	0.03	-0.10	0.10	0.14	0.01	-0.14	-0.12	-0.04
Kinase inhibitor	-0.33	-0.84	-0.87	-0.62	-0.50	-0.95	-0.80	-0.07
Nuclear receptor ligand	0.20	0.23	0.15	0.17	0.21	0.33	-0.24	-0.19
Protease inhibitor	0.15	-0.71	-0.65	-0.63	-0.05	-0.70	-0.72	-0.21
Enzyme inhibitor	0.38	0.29	0.27	0.45	0.29	0.27	-0.14	0.28

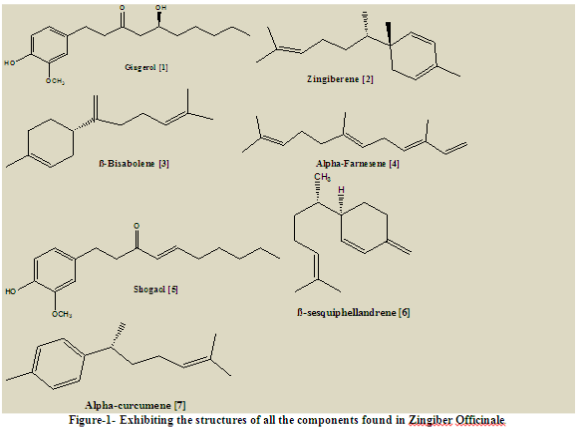

Figure-1- Exhibiting the structures of all the components found in Zingiber Officinale

CONCLUSION

The Zingiber officinale extract was achieved and subjected for antimicrobial screening that showed methanol extract has better potential than hexane. Phytochemical analysis to confirm the composition were obtained from the literature and all the components were evaluated for drug likeness, physicochemical, and molecular docking parameters. Drug likeness score revealed that all the components possess good score except component seven but in case of physicochemical parameter four components were found against the Lipinski rule. Molecular docking evaluation strongly recommended the results obtained experimentally.

REFERENCES

1. WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR). Antimicrobial resistance: global report on surveillance 2014; April 2014.
2. Triyana, S.Y., 2009. Antibiotic resistance of pathogenic bacteria. KESPHA 1, 92-94.
3. David K. Henderson, American Journal of Infection Control, 2006; 34: S46-54.
4. Fred C. Tenover, American Journal of Infection Control, 2006; 34: S3-10.
5. Kane, J.H., Finlay, A.C., Sobin, B.A., 1950. Antimicrobial agents from natural sources. Ann. NY Acad. Sci. 53: 226-228.
6. Gyawali R, Salam AI. Natural products as antimicrobial agents. Journal of food and drug analysis, 2015; 23: 417-424.
7. Krishnaiah D, Sarbatly R, Nithyanandam R. A review of the antioxidant potential of medicinal plant species. Food Bioprod Process, 2011; 89: 217-33.
8. Luo Y, Cai Q, Sun M, Corke H. Antioxidant activity and phenolic compounds of 112 traditional Chinese medicinal plants associated with anticancer. Life Sci, 2004; 74: 2157-84.
9. Kumar S, Bajwa BS, Singh K, Kalia AN. Anti e inflammatory activity of herbal plants: a review. Int J Adv Pharm Biol Chem 2013; 2: 272-81.
10. Atta-Ur-Rahman, Zaman K. Medicinal plants with hypoglycemic activity. J Etnopharmacol 1989; 26: 1-55.
11. Ensminger AH, Ensminger ME, Kondale JE, Robson JRK. Foods & nutrition encyclopedia. Clovis; California, USA: Pegus Press; 1983.
12. Demin G, Yingying, Z (2010) Comparative antibacterial activities of crude polysaccharides and flavonoids from Zingiber officinale and their extraction. American Journal of Tropical Medicine 5: 235-238.
13. Sasidharan I, Nirmala Menon A (2010) Comparative Chemical Composition and Antimicrobial Activity Fresh & Dry Ginger Oils (Zigiber Officinale Roscoe). International Journal of Current Pharmaceutical Research, 2: 40-43.
14. Sebiomo A, Awofodu AD, Awosanya AO, Awotona FE, Ajayi AJ (2011) Comparative studies of antibacterial effect of some antibiotics and ginger (Zingiber officinale) on two pathogenic bacteria. Journal of Microbiology and Antimicrobials 3: 18-22.
15. Lee YB, Kim YS, Ahmore CR (1986) Antioxidant property in ginger rhizoma and its application to mate products. Journal of Food Science 51: 20-23.
16. Penna SC, Medeiros MV, Aimbire FS, Faria-Neto HC, Sertié JA, et al. (2003) Anti-inflammatory effect of the hydralcoholic extract of Zingiber officinale rhizomes on rat paws and skin edema. Phytomedicine 10: 381-385.
17. Kadnur SV, Goyal RK (2005) Beneficial effects of Zingiber officinale Roscoe on fructose induced hyperlipidemia and hyperinsulinemia in rats. Indian J Exp Biol, 43: 1161-1164.
18. Islam MS, Choi H (2008) Comparative effects of dietary ginger (Zingiber officinale) and garlic (Allium sativum) investigated in a type 2 diabetes model of rats. J Med Food, 11: 152-159.
19. Kim JS, Lee SI, Park HW, Yang JH, Shin TY, et al. (2008) Cytotoxic components from the dried rhizomes of Zingiber officinale Roscoe. Arch Pharm Res, 31: 415-418.
20. Isa Y, Miyakawa Y, Yanagisawa M, Goto T, Kang MS, et al. (2008) 6-Shogaol and 6-gingerol, the pungent of ginger, inhibit TNF-a mediated down regulation of adiponectin expression via different mechanisms in 3T3-L1 adipocytes. Biochem and BiophyS ReS Commun, 373: 429-434.
21. Wang W, Li CY, Wen XD, Li P, Qi LW (2009) Simultaneous determination of 6-gingerol, 8-gingerol, 10-gingerol and 6-shogaol in rat plasma by liquid chromatography–mass spectrometry: Application to pharmacokinetics. J Chromatogr B Analyt Technol Biomed Life Sci B, 877: 671-679.
22. Shim S, Kim S, Choi DS, Kwon YB, Kwon J (2011) Anti-inflammatory effects of [6]-shogaol: Potential roles of HDAC inhibition and HSP70 induction. Food Chem Toxicol, 49: 2734-2740.
23. Akoachere, J.F., Ndip, R.N., Chenwi, E.B., Ndip, L.M., Njock, T.E., Anong, D.N., 2002. Antibacterial effect of Zingiber officinale and Garcinia kola on respiratory tract pathogens. East Afr. Med. J. 79: 588-592.
24. Reddy, A.C., Lokesh, B.R., 1992. Studies on spice principles as antioxidants in the inhibition of lipid peroxidation of rat liver microsomes. Mol. Cell. Biochem, 111: 117-124.
25. Vimala, S., Norhanom, A.W., Yadav, M., 1999. Anti-tumor promoter activity in Malaysian ginger rhizome used in traditional medicine. Br. J. Cancer 80: 110-116.
26. Rahmani AH, Shabrmi FM, Aly SM. Active ingredients of ginger as potential candidates in the prevention and treatment of diseases via modulation of biological activities. Int J Physiol Pathophysiol Pharmacol, 2014; 6: 125-36.
27. Choudhari SS, Kareppa BM. Identification of bioactive compounds of zingiber officinale roscoe rhizomes through gas chromatography and mass spectrometry. Int J Pharm Res Dev, 2013; 5: 16e20.
28. Sooad Al-Daihan, Manar Al-Faham, Nora Al-shawi, Rawan Almayman, Amal Brnawi, Seema zargar, Ramesa shafi Bhat, Antibacterial activity and phytochemical screening of some medicinal plants commonly used in Saudi Arabia against selected pathogenic microorganisms, Journal of King Saud University-Science, April 2013; 25(2): 115–120.
29. S.P Malu, G.O Obochi, E.N Tawo, B.E Nyong, Antibacterial activity and medicinal properties of ginger (Zingiber officinale), Global Journal of Pure and Applied Sciences Vol. 2009; 15(3-4) .

30. Ponmurugan Karuppiah, Shyamkumar Rajaram, Antibacterial effect of Allium sativum cloves and Zingiber officinale rhizomes against multiple-drug resistant clinical pathogens, Asian Pac J Trop Biomed. 2012 Aug; 2(8): 597-601.
31. Kamrul Islam, Asma Afroz Rowsni, Md. Murad Khan and Md. Shahidul Kabir, Antimicrobial activity of ginger (zingiber officinale) extracts against food-borne pathogenic bacteria, International Journal of Science, Environment and Technology, 2014; 3(3): 867-871.
32. Gisele Mara Silva Gonçalves, Gustavo Henrique da Silva, Pedro Paulo Barros, Silvana Mariana Srebernich, Fernanda Rocha Tonon, Daniella Souza Fiore, Antimicrobial effect and enzymatic activity of extract of Zingiber officinale Roscoe and stability in topical preparations, Rev Ciênc Farm Básica Apl., 2014; 35(2): 205-210.
33. Hiba Ali Hasan, Ayad Mohammed Rasheed Raauf, Basama Monjd Abd Razik and Bassam Abdul Rasool Hassan, Chemical Composition and Antimicrobial Activity of the Crude Extracts Isolated from Zingiber Officinale by Different Solvents, Pharmaceut Anal Acta 2012; 3: 9.
34. Mohammad Arshad, Abdul Roouf Bhat, Kwon Kang Hoi, Inho Choi, Fareeda Athar, Synthesis, characterization and antibacterial screening of some novel1,2,4-triazine derivatives. **http://dx.doi.org/10.1016/j.cclet.2016.12.037.**
35. Abdul Kareema, Laxmi, Mohammad Arshad and Nahid Nishat. Herbo-Mineral based Schiff base ligand and its metal complexes: synthesis, characterization, catalytic potential and its biological applications. Journal of Photochemistry and Photobiology B: Biology. 2016; 160: 163-171.
36. Noor e Iram, Mohd Shoeb Khan, Reshma Jolly, Mohammad Arshad, Mahboob Alam, Parvez Alam, Rizwan Hasan Khan, Farha Firdaus, Interaction mode of polycarbazole-titanium dioxide nanocomposite with DNA: Molecular docking simulation and in-vitro antimicrobial study. Journal of Photochemistry and Photobiology B: Biology. 2015; 153: 20-32.
37. Rani Bushra, M. Shahadat, Meraj Alam Khan, R. Adnan, Mohammad Arshad, M. Rafatullah and Mu. Naushad, Preperation of Polyaniline based Nanocomposite material and their Environmental Applications. 2014, Int. J. Env. Sci. Technol.
38. Mohammad Arshad, Tazeem, A R Bhat, Fareeda Athar, Heterocyclic Azoles and their biological application as antimicrobials. Journal of Natural Science, Biology and Medicine, 2011; 2(2): 1-156.
39. Tazeem, Mohammad Arshad, A R Bhat, Fareeda Athar, Synthesis, characterization of heterocyclic compounds and their application as antibacterial therapeutic agents. Journal of Natural Science, Biology and Medicine, 2011; 2(2): 1-156.
40. Tuhfa, Mohammad Younus Wani, Mohammad Arshad, Tazeem, Fareeda Athar, Chalcone scaffold: Synthesis, modification, characterization, molecular properties and screening against microbes. Journal of Natural Science, Biology and Medicine, 2011; 2(2): 1-156.
41. Alodeani E A, Arshad M, Izhari M A: Anti-uropathogenic activity, drug likeness, physicochemical and molecular docking assessment of (E-)-N' -(substitutedbenzylidene)-2-(quinolin-8-yloxy) acetohydrazide. Asian Pac J Trop Biomed 2015; 5(8): 676-683.
42. Nova ulica: Molinspiration cheminformatics [homepage on the internet], SK-900 26 Slovensky Grob, Slovak Republic [cited 2012 July3], Available from http://www.molinspiration.com.
43. Verma, A: Lead finding from Phyllanthus debelis with hepatoprotective potentials Asian Pacific Journal of Tropical Biomedicine 2012; S1735-S1737.
44. Lipinski CA, Lombardo F, Dominy BW, Feeney PJ: Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Adv. Drug Delivery Rev. 1997; 23(1-3): 3-25.
45. Alodeani E A, Arshad M, Izhari M A: Anti-uropathogenic activity, drug likeness, physicochemical and molecular docking assessment of (E-)-N' -(substitutedbenzylidene)-2-(quinolin-8-yloxy) acetohydrazide. Asian Pac J Trop Biomed 2015; 5(8): 676-683.
46. Alodeani E A, Arshad M, Izhari M A: Antileishmanial screening, physicochemical properties and drug likeness of pyrazole carbaldehyde derivatives: Asian Pac. J. Health Sci. 2015; 2(2): 41-47.
47. Alodeani E A, Arshad M, Izhari M A: Antileishmanial activity and computational studies of some hydrazone derivatives possessing quinoline nucleus. European Journal of Pharma and medical research. 2015; 2(7): 324-328.
48. Alodeani E A, Arshad M, Izhari M A: Drug likeness and physicochemical properties evaluation of the alkaloids found in black pepper: piperine, piperidi ne, piperettine and piperanine. European Journal of Pharma and medical research 2015; 2(6): 296-301.