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Exploring Bioactive Compounds in Anti-Microbial Herbs: Antifungal and Antibacterial Evaluation for Drug Discovery

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Abstract

Antimicrobial resistance became in the last two decades a global threat to public health systems in the world, therefore, there is a continuous movement to find new drugs to replace those that have been resisted by microbes, especially in the field of fungal and yeast drugs. There are known diseases associated with the growth of these organisms in human bodies. This study aimed to explore and evaluate the effectiveness of natural herbs as antimicrobial agents, with a focus on their potential as alternatives or complements to traditional drugs in light of the increasing microbial resistance to current treatments. Eleven herbs (Pomegranate peel, thyme, Lemongrass, Cinnamon, Coriander, Cumin, olive leaf, Licorice, Garlic, Apple vinegar, turmeric) with known antimicrobial properties were selected based on a historical heritage and they were examined using pathogenic creatures. The eleven herbs were prepared in the laboratory just as they are prepared in various societies as antimicrobial herbs.

The results revealed that four of the eleven herbs exhibited significant antimicrobial activity, in some cases surpassing the effectiveness of currently available drugs as fluconazole. The active compounds in these herbs were identified for finding a suitable explanation for the effectiveness of the different compounds in these four herbs, and they show promise for use either independently or with chemical modifications to enhance their efficacy.

Different compounds of four effective herbs were characterized using the Gas chromatography/mass spectrometry (GC/MS) apparatus. In addition, MIC (Minimum Inhibitory concentration) and MFC (Minimum fungicidal concentration) for them were done.

Keywords*: Medicinal herbs, anti-microbial, Drug resistant, new treatments.*

1. Introduction

Unprecedented is the rate at which pathogenic fungi that are resistant to the few widely used antifungal medications are emerging. For instance, azoles are utilized in timber preservation, antifouling coatings, crop protection, and the treatment of human and animal health. In many situations, the independent evolution of resistance has been accelerated by the widespread usage and versatility of azoles. One effect of this is that opportunistic fungal diseases that exist naturally and have developed resistance to this wide class of drugs pose a growing risk to human health. Improved management of already available chemicals, the advancement of novel antifungal discoveries, and preventive measures are necessary to prevent a global collapse in our capacity to control fungal infections and to prevent catastrophic failures in medical and food security [1-13].

The fungal pathogens Candida albicans, Cryptococcus neoformans and Aspergillus fumigatus cause a total of more than 1 million deaths each year. Long-term use of antifungal drugs can easily lead to fungal resistance, and the prevalence of drug-resistant fungi is a major global health challenge [14-17]. Fungal pathogens cause significant human morbidity and mortality globally, where there is a propensity to infect vulnerable people such as the immunocompromised ones. There is increasing evidence of resistance to antifungal drugs, which has significant implications for cutaneous, invasive and bloodstream infections [18-20]. The currently available antifungals have many limitations, including poor oral bioavailability, narrow therapeutic indices, and emerging drug resistance resulting from their use, thus making it essential to investigate the development of novel drugs which can overcome these limitations and add to the antifungal armamentarium [21].

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In this study, most herbs that used for thousands of years were tested against pathogenic Bactria and fungi. Just four of them are still active whereas other not. According to this study the chemical structures of GC-MS apparatus of different compounds

2. Results and Discussion

Biological activity of all herbs was done by agar well diffusion method, wells about 5 millimeters in Nutrient agar about four wells for each Petri dish. The inhibition zone in millimeter of each herb of 11 herbs as in the following figures:

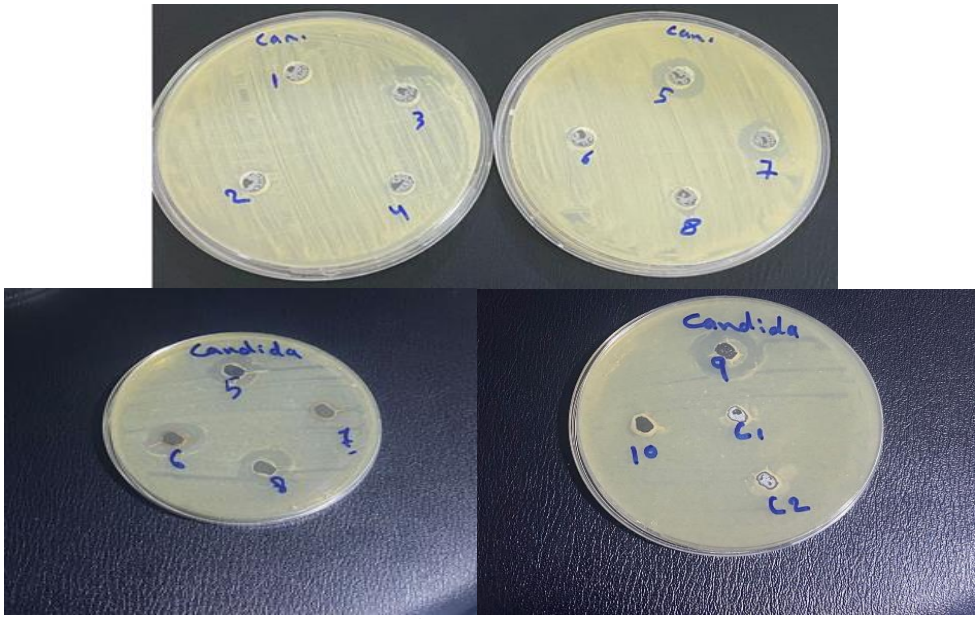


Figure (1): Inhibition Zones of 11 medicinal herbs against candida albicans.

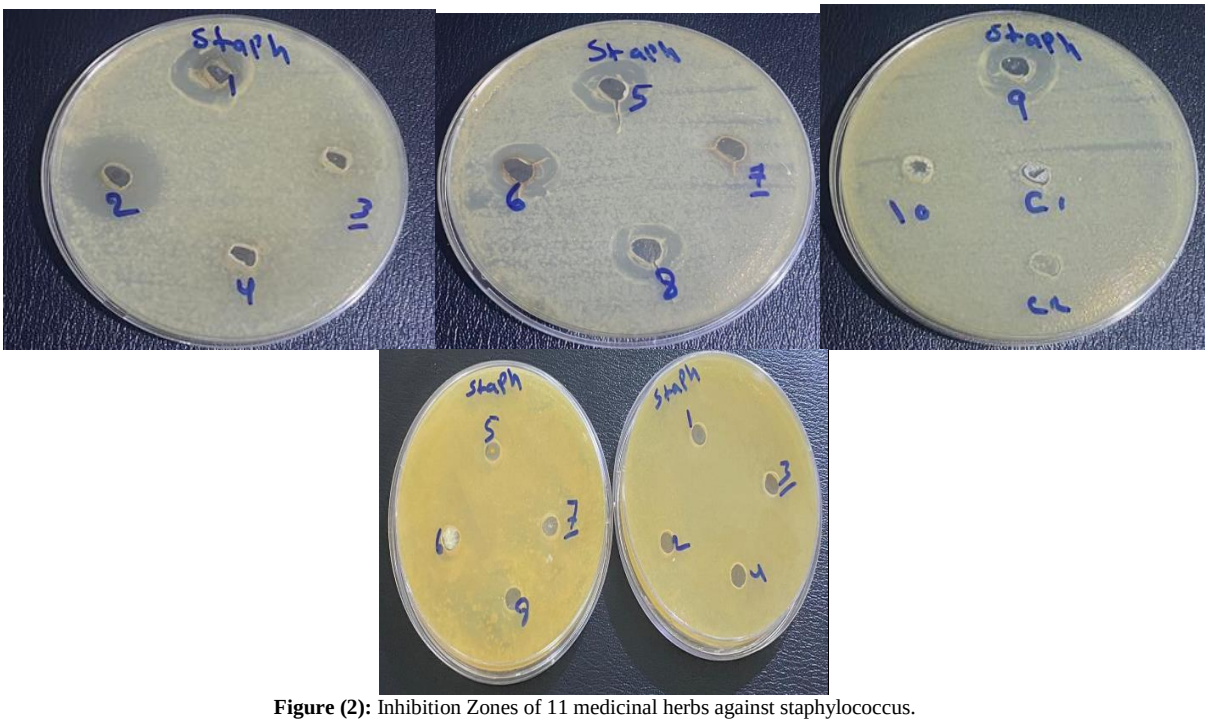


Figure (2): Inhibition Zones of 11 medicinal herbs against staphylococcus.

Where: both figures have same numbers which are two groups (1-10) group while (1-8) another group.
(1-10) group are:
(1-2) = Pomegranate peel.
(3) = Thyme
(4) = Lemongrass
(6-7) = Cinnamon.
(8-9) = Coriander.
(10) = Cumin
Note: No. (5) (Basil) has been neglected because it is seasonal and not available in the market but it was showed high biological activity against both organisms' candida and Staphylococcus.

The other group (1-8) are:
(1) = Olive leaf.
(2) = Licorice.
(3) = Garlic.
(4) = Apple Vinegar.
(5) = Turmeric.
(6) = Nystatin drug.
(7) = Fluconazole drug.
(8) = Ethanol.

While the results in millimeters of inhibition zone against candida albicans and staphylococcus aureus for both groups are as in the following tables:

Table (1): Represent the results of biological activity of some herbs.

Herb's name		**Pomegranate peel in distilled water**	**Pomegranate peel in acetone 50% with pH=2-2.5**	**thyme**	**Lemongrass**	**Cinnamon in boiling water**	**Cinnamon in cold water for 24 hr.**	**Coriander in boiling water**
Inhibition zone (in millimeter)	**pathogenic Candida albicans (fungi)**	**13**	**16**	**R***	**R**	**15**	**R**	**14**
	pathogenic Staphylococcus aureus (bacteria)	**14**	**15**	**R**	**R**	**11**	**R**	**12**

Table (2): Represent the results of biological activity of rest herbs with the drugs.

Herb's name		**Coriander in acetone**	**Cumin**	**olive leaf**	**Licorice**	**Garlic**	**Apple vinegar**	**turmeric**	**Nystatin drug**	**Fluconazole drug**
Inhibition zone (in millimeter)	**pathogenic Candida albicans (fungi)**	**15**	**R**	**R**	**R**	**R**	**R**	**15**	**R**	**13**
	pathogenic Staphylococcus aureus (bacteria)	**14**	**R**	**R**	**R**	**R**	**R**	**R**	**R**	**R**

One of the important issue that in this study it was prepared the solutions of medicinal herbal exactly as people prepare them in different communities and in natural situations. That is, when they use them to treat multiple fungal infections. It may have mentioned in this study all the herbs used as antifungals, including Candida yeast.

According to the two above tables (1 and 2), they showed the problem that many researchers around the world are searching for solutions for it for the last fifty years, which is finding new medicines as antifungal treatment due to the resistance of different fungi including Candida yeast and other organisms to many different medicines and treatments. The best evidence of this issue that the two tables above; 11 different herbs dedicated to be anti-fungi while Candida resisted and many of them were lost. Just 4 of them are still active while 7 have no effectiveness, that is, more than half of the herbs. In addition, this study also used two well-known and widely used medicines Nystatin and Fluconazole, one of which showed effectiveness and the other did not.

In this study and as it is obvious from above tables, pathogenic yeast was used, not standard, and the reason of this the results to be real and realistic against deceptive organisms that are mainly present in the human intestines, and not standard organisms that have no relation to reality and the many effects that they secrete, which have been explained previously.

In fact, these herbs are considered a summary of very ancient medicine and are the result of many experiments. What is certain is that they are the result of a living experiment even this they were resisted by fungi in general and Candida in particular. Therefore, these facts put science and scientists at a crossroads, either finding new successful treatments or surrendering to these organisms. Laboratory's staff in medical field believed that there is no successful treatment for fungi, and this is an abnormal issue that must be addressed. Therefore, this study will present different solutions that may provide a wide scope for finding new treatments for fungi and for candida.

The 4 herbs that gave good results against Candida yeast were studied, and they were; pomegranate peels with two compounds of different statuses, cinnamon, coriander and Turmeric.

Actually, there are two important points that must be paid attention to, which is that turmeric shows high effectiveness against Candida, but it does not show effectiveness against bacteria, unlike the rest of the effective herbs. Furthermore, this is more important, all herbs, as is clear from the two tables above, show effectiveness against Candida that is higher than the effectiveness of the drug Fluconazole which is currently used as an antifungal, and this gives hope for finding new medicines stronger than what is available. It is well known that the compounds resulting from the above herbs can be modified to make them stronger than they are, and thus may be find more than one successful treatment against fungi in general and Candida in particular.

It is difficult to predict which of the compounds below has the highest effectiveness against Candida yeast. This is because each drug targets a specific part of this yeast, and there are drugs that decompose according to their metabolism within the body, producing drugs that are smaller in molecular weight and may be stronger or weaker as antifungals. Also, one or two compounds may intervene more in the fungal inhibitor, which makes the prediction process very difficult, but from studying all the following structures, a good group may have extracted is effective.

However, above active herbs contain many different molecules one or more of them may be effective against fungi or candida while the rest are not. Then the chemical structure of these molecules according to GC-Ms results and an estimate of the effective molecules will also be shown below also the sequence of herbs and compounds they contain is as follows:

1= Pomegranate peel in distilled water.
2= Pomegranate peel in acetone 50%.
3= Coriander in boiling water.
4= Cinnamon in boiling water.
5= Turmeric.

1. **Pomegranate peel in distilled water**: following table should illustrate what this herb contain which are 9 different molecules as following table:

Table (3): Different compounds that Pomegranate peel in distilled water contain.

No.	Name of the compounds	Notes
1	TETRACOSAMETHYLCYCLODODECASILOXANE	
2	Iron, monocarbonyl-(1,3-butadiene-1,4-dicarbonic acid, diethyl ester) a,a'-dipyridyl	
3	Phosphonic acid, dioctadecyl ester	
4	BISTRIMETHYLSILYL N-ACETYL EICOSASPHINGA-4,11-DIENINE	
5	Cyclononasiloxane, octadecamethyl	
6	TETRACOSAMETHYLCYCLODODECASILOXANE	
7	Pentasiloxane, dodecamethyl	
8	Octasiloxane, 1,1,3,3,5,5,7,7,9,9,11,11,13,13,15,15-hexadecamethyl	
9	4-[4-Amidoximinothiophenoxy]benzaldehyde ethylene acetal	

Note: Should be noted that the molecules numbers above in the above table are the same for the molecules as follows:

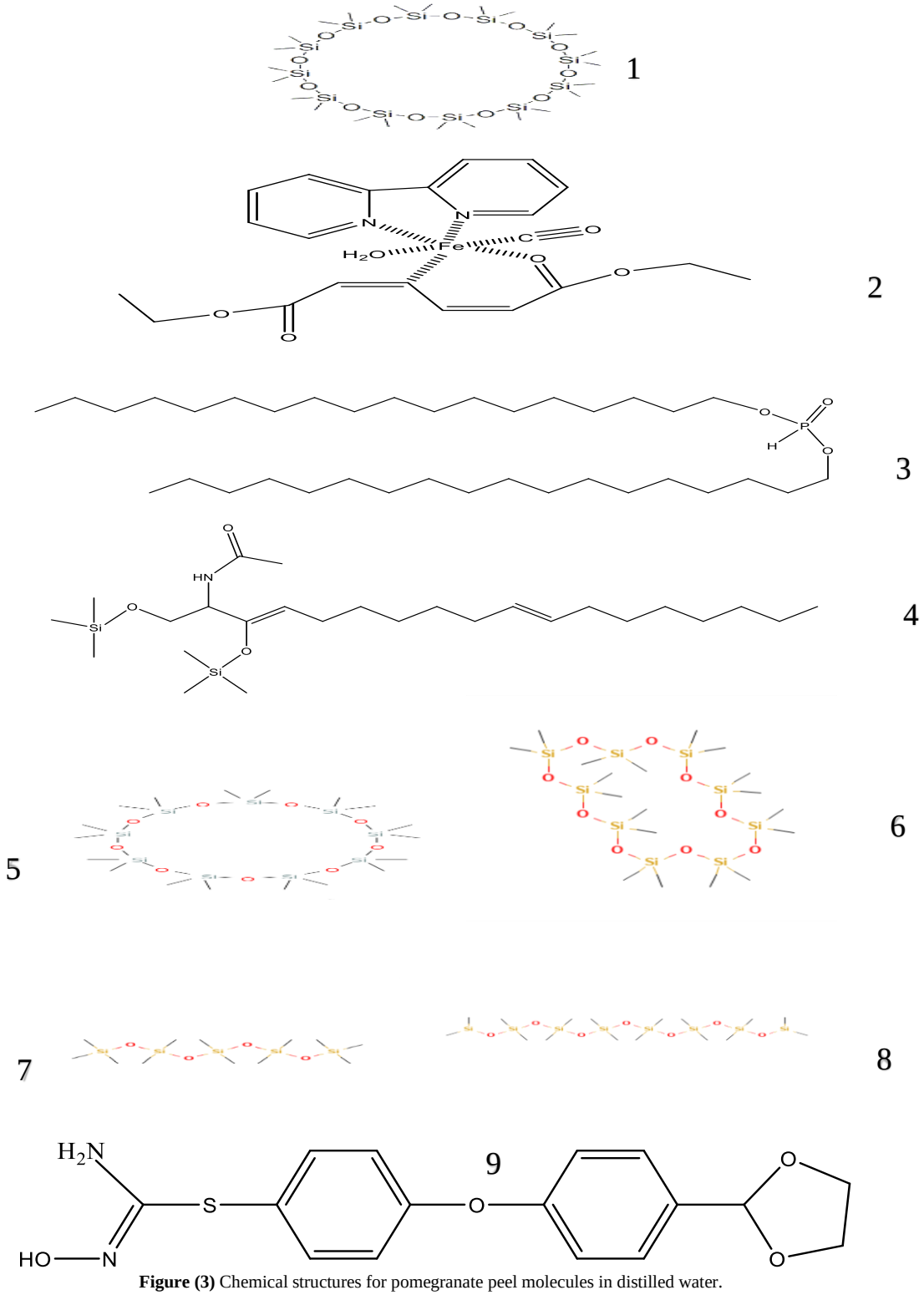
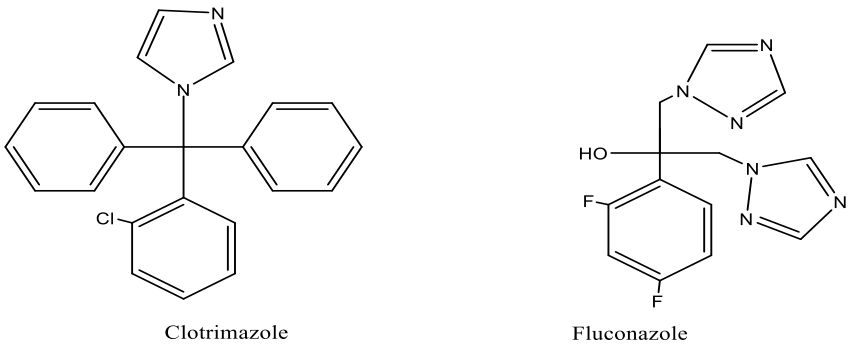


Figure (3) Chemical structures for pomegranate peel molecules in distilled water.

For studying these nine chemical forms, a comparison with chemical structure of known anti-Candida drugs may lead to find the active molecule or molecules, which are:



Clotrimazole Fluconazole

Figure (4): Chemical structure of Fluconazole and Clotrimazole anti-candida drugs.

Therefore, due to two nitrogen atom in 2 and 9 compounds may they have good properties as antimicrobial agents. In addition, Silicon atom is a good agent as antibacterial. Furthermore, 3 and 4 molecules are good molecules as anti-candida agent and this will be so clear in last herb. Following molecules are stronger than above molecules:

2- **Pomegranate peel in acetone 50% with pH=2-2.5**: it has just two molecules as in the following table:

Table (4): Different compounds that Pomegranate peel in in acetone 50% contain.

No.	Name of the compounds	Notes
1	1,2-Benzenedicarboxylic acid, 3-nitro	
2	Di(2-ethylhexyl) isophthalate	

Pomegranate peel here just two molecules and more activity than above same herb in distilled water as table (1) show. These compounds (1 and 2) have good properties as antimicrobial and show this property so clear. Therefore, they should be a new line as antibacterial or antifungal agents. And also above number of the two compounds as same as following compounds:

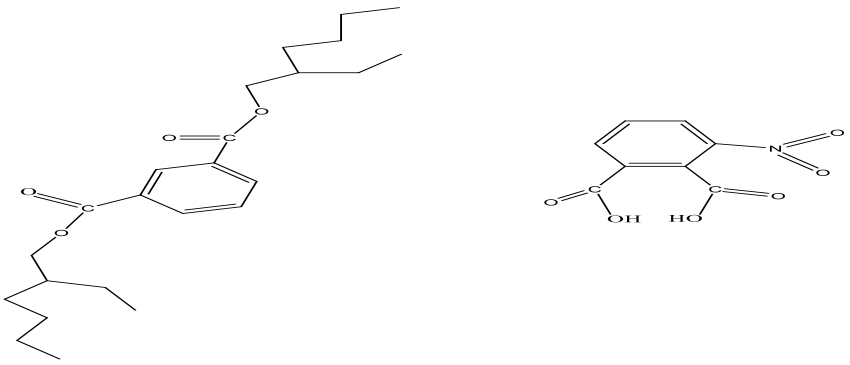


Figure (5) Chemical structure of Pomegranate peel molecules in acetone 50%.

As it is notice the four hydrocarbon arms of above compound 2, and this is what it was seen in compounds 3 and 4 of the previous compounds figure (3-1), it is obvious arms that give this herb its activity.

3. **Cinnamon**: It gives three different molecules as in the following table:

Table (5): Different compounds that Cinnamon contain.

No.	Compounds name	Notes
1	β-Gurjunene	
2	acrylic acid tetradecanyl ester	
3	16-Allopreganene-3-ol-20-one	

Chemical structure of above molecules is in the following also the numbers as in above table:

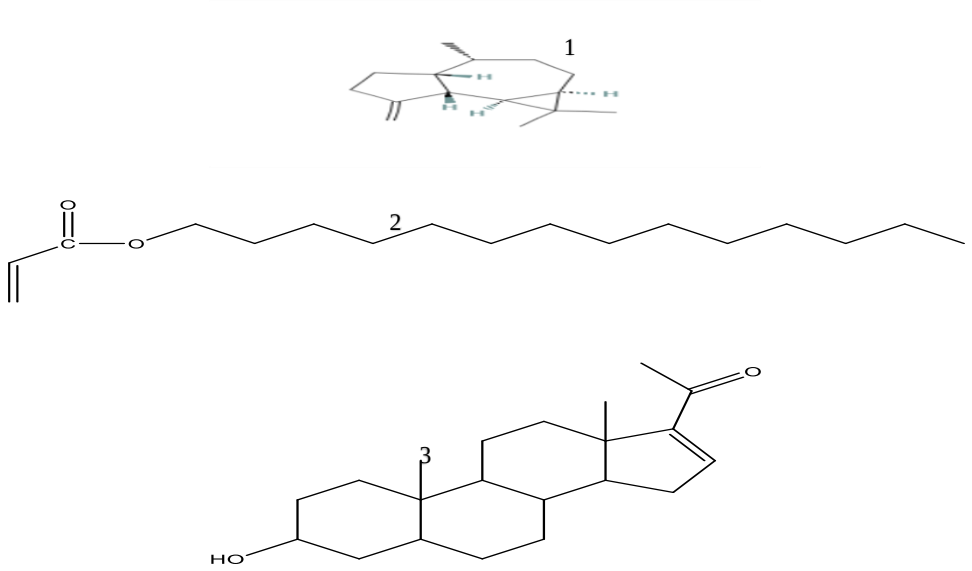


Figure (6): Chemical structures of Cinnamon's compounds.

This herb (Cinnamon) gives higher inhibition zone than known antifungal drug Fluconazole as shown before and this due to compound (2) which may present new line of antifungal drug or antibacterial agent.

4. **Coriander**: this herb gives 18 different molecules as following table:

Table (6): Different compounds that Coriander contain.

No.	The Compound name	Notes
1	Bicyclo[3.1.1]hept-2-ene, 2,6,6-trimethyl-, (.+/-.)-	
2	Silane, [3-(2,3-epoxypropoxy)propyl]ethoxydimethyl-	
3	.gamma.-Terpinene	
4	LINALOOL L	
5	Disiloxane, pentamethyl-	
6	S-1-Phenyl-1-pentyn-3-ol	
7	5,4'-Dimethoxy-2-methylbibenzyl	
8	3,4,8-trimethyl-9-oxy-1-trimethylsilyloxybicyclo[4.3.1]non-1-ene	
9	Phenol, 2,6-bis(1,1-dimethylethyl)-4-methyl-	
10	Guanosine	
11	3aH-Inden-3a-ol, octahydro-1,4,4,7a-tetramethyl-, (1.alpha.,3a.beta.,7a.alpha.)-	
12	9-Octadecenamide, (Z)-	
13	Bis(2-ethylhexyl) phthalate	
14	.beta.-Monoolein	
15	.gamma.-Sitosterol	
16	Octasiloxane, 1,1,3,3,5,5,7,7,9,9,11,11,13,13,15,15-hexadecamethyl-	
17	Heptasiloxane, 1,1,3,3,5,5,7,7,9,9,11,11,13,13-tetradecamethyl-	
18	Stigmast-4-en-3-one	

As same as above herbs the number of above compounds in above table are same as the number of each molecules as following structures:

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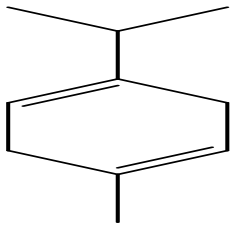

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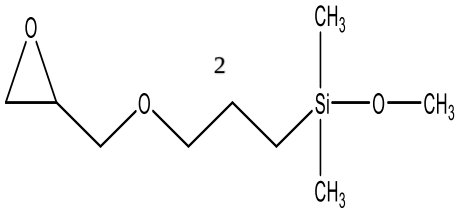

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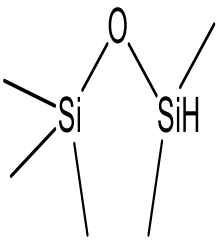

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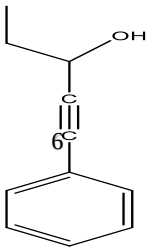

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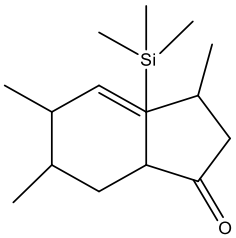

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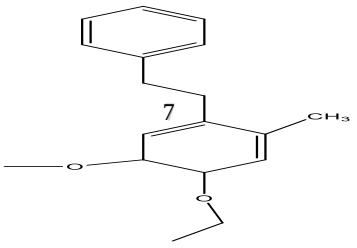

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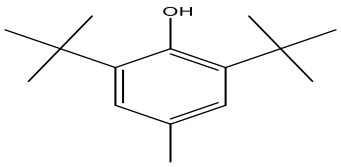

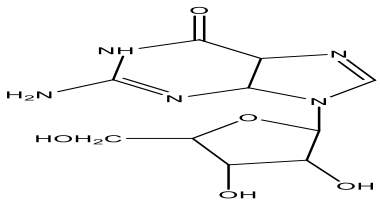

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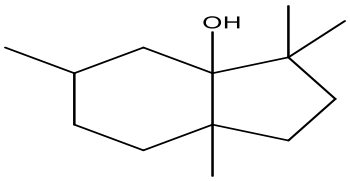

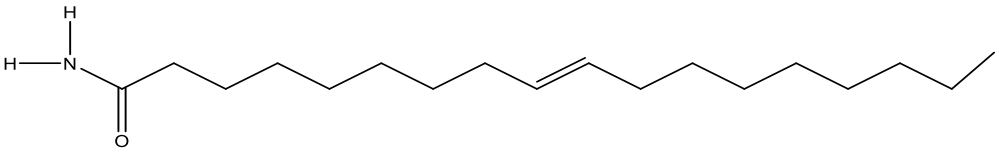

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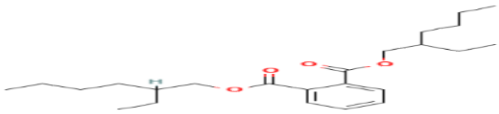

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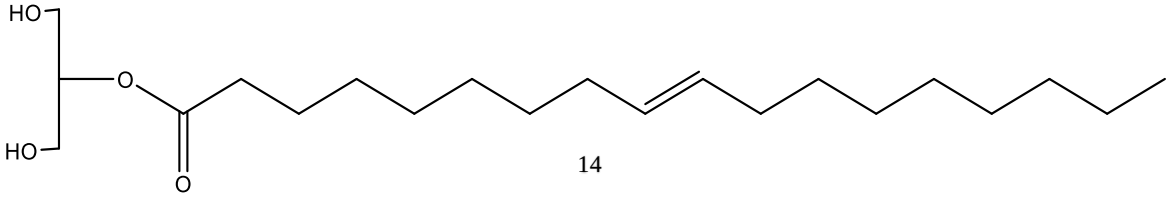

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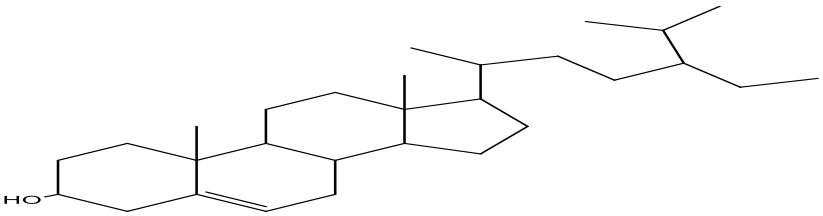

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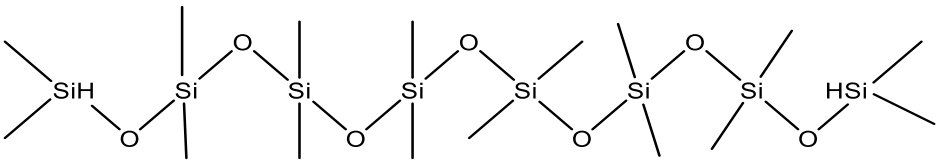

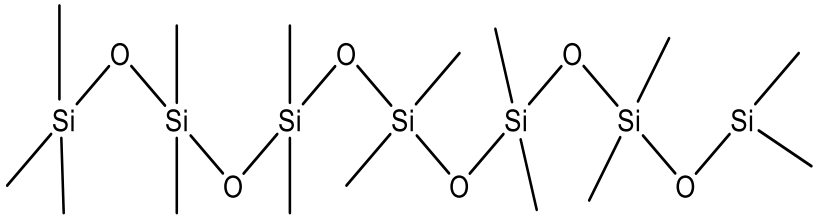

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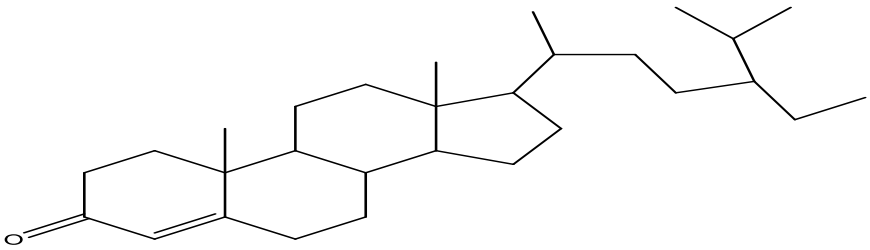

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Figure (7): Chemical structures of Coriander's compounds.

It is worth noting that antifungals drugs are few, and many of them, as it was illustrated before in case of Nystatin known antifungal drug, have been resistant to the fungi. Likewise, introducing new drugs has become difficult. Therefore, this study presented production lines for new drugs that are effective against pathogenic fungi and can be modified in laboratories to become stronger than they are. In order to present a new line of antifungal medicine.
As it mentioned before, above compounds 12, 13, 14, 15 and 18 have a chain or chains of carbon atoms so the activity of Coriander may due to them. In addition, other compounds may have additional activity.

5- Turmeric: This herb showed activity against fungi, but it did not show effectiveness against bacteria and the compounds it contains, as in the following table:

Table (7): Different compounds that Turmeric contain.

No.	The compounds Turmeric has	Notes
1	11,14-Octadecadienoic acid, methyl ester	
2	Cyclohexene, 4-(4-ethylcyclohexyl)-1-pentyl	
3	10, 13-Octadecadienoic acid, methyl ester	

As shown before the number of each compound as same as following figures:

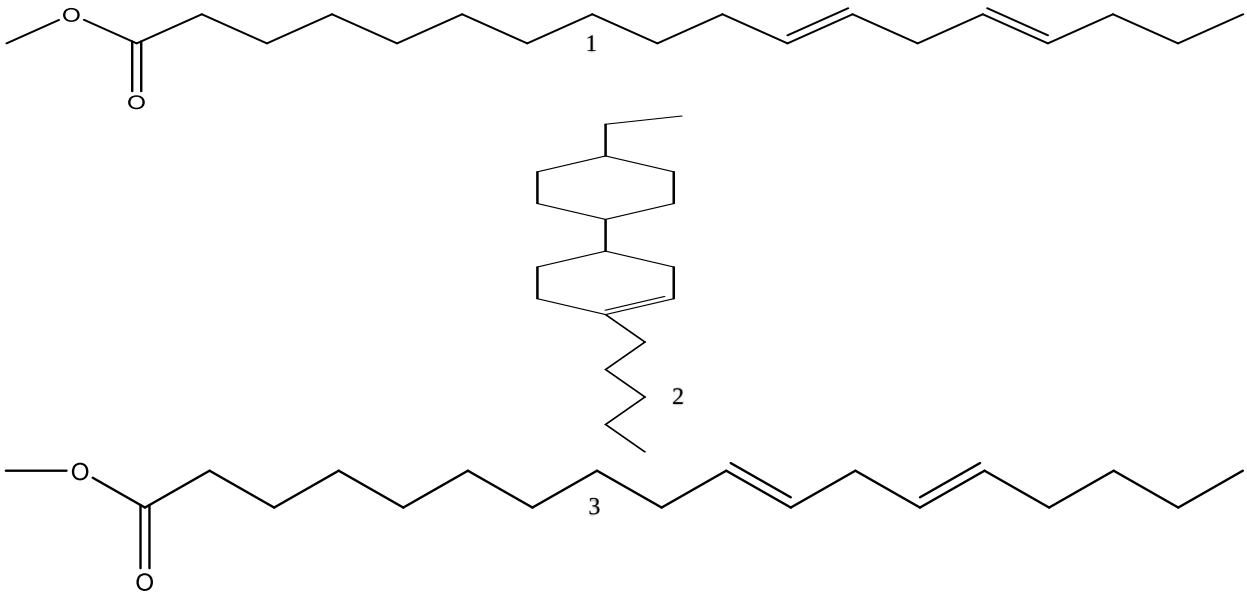
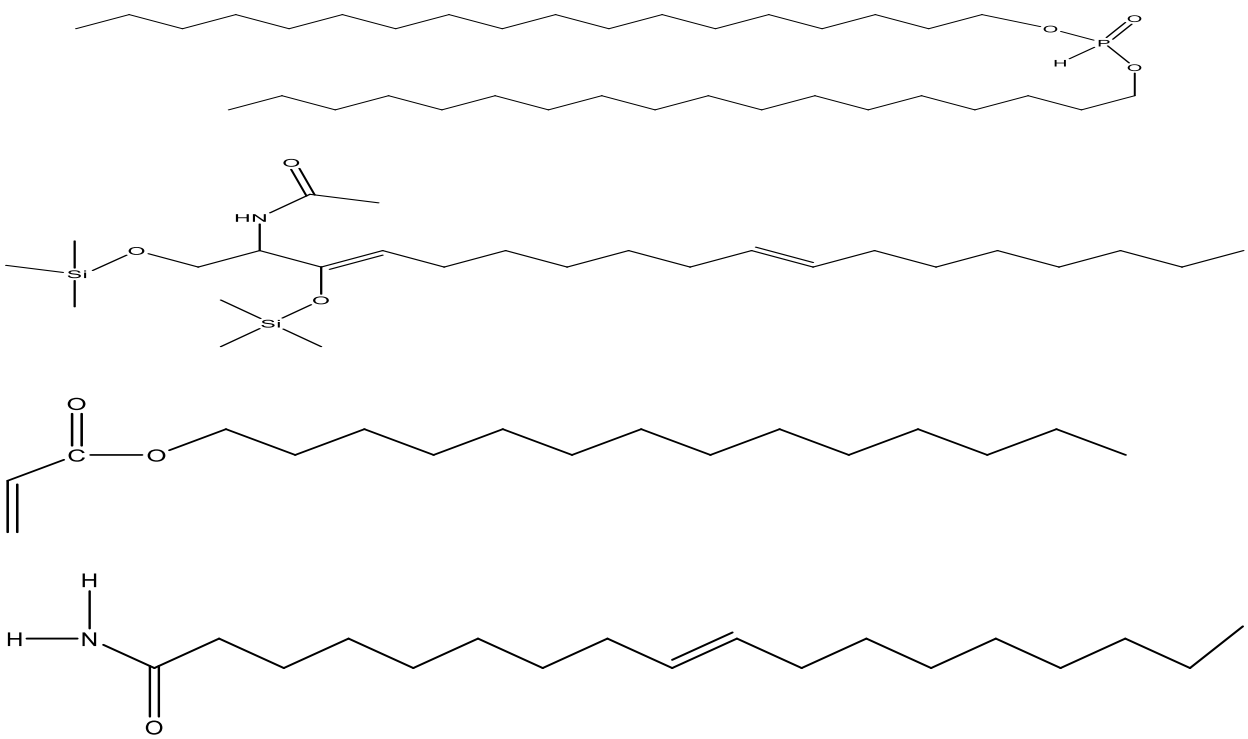
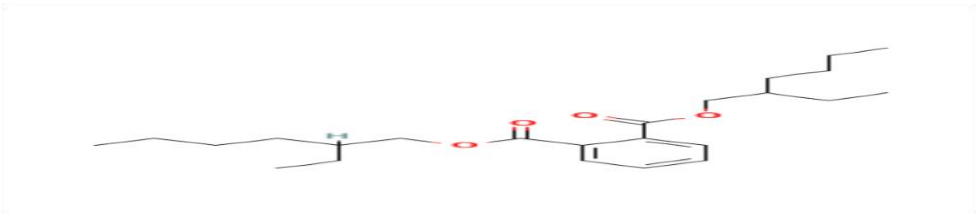
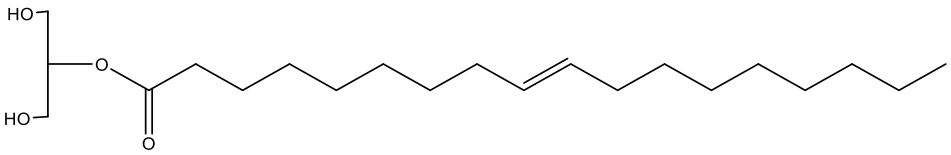


Figure (8): Chemical structures of Turmeric's compounds.

This herb has wide inhibition zone than known antifungal drug "Fluconazole", the three above compounds are new antifungal agents especially 1 and 3. These compounds as shown before strong agents as antifungal.
From the last herb "turmeric" that it is antifungal and not antibacterial because the chemical structures of its three compounds demonstrate what it was seen previously about the chain or chains of carbon atoms and their relationship with inhibiting fungi or Candida yeast.
Also, one of the important observations is that previous herbs they give high inhibition zone as antifungal and antibacterial and they contain both groups, especially coriander. Thus, the group of carbon chains is antifungal or anti-Candida, while the rest of the compounds are considered antibacterial. Thus, this study presents two types of drugs antifungals and antibacterial.
In order to clarify the issue of the carbon chain or chains, a collection of them are below in order to make it possible to clarify this topic:



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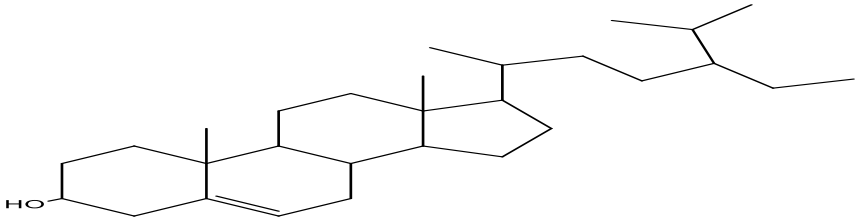
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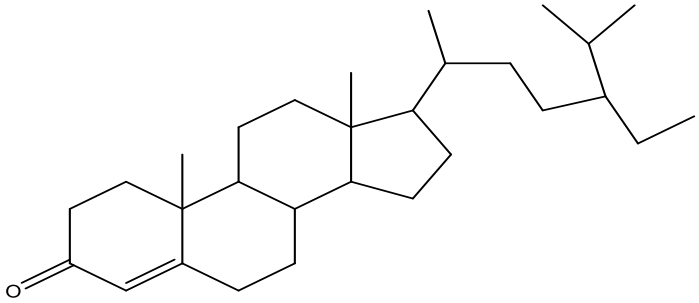
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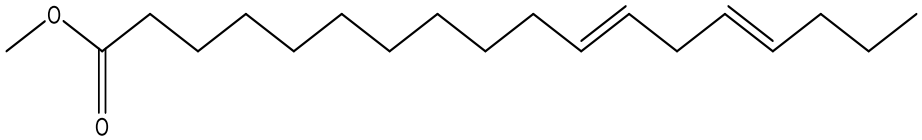
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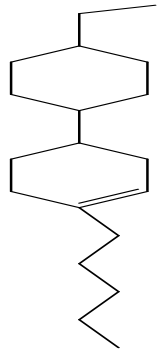

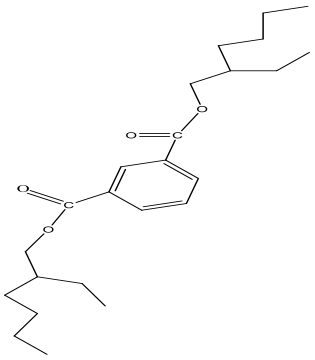
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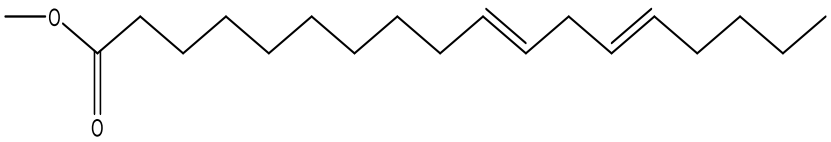


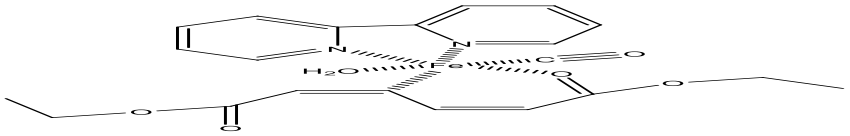
Figure (9): Chemical structures of chain or chains carbon atoms compounds.

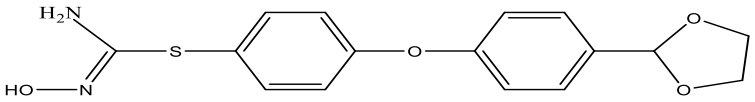
These compounds gave high effectiveness against Candida in particular and fungi in general, and gave a higher effectiveness than the drug Fluconazole, as was explained previously. Therefore, they were listed above, not according to their order in the herbs, but collecting them randomly, and the important thing is that the reason for their effectiveness must be

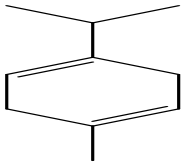
This was showed before that Candida yeast secretes three important compounds; lipases, protease and hemolysin (Candidalysin). These molecules hydrolyze most molecules except one! actually no molecule can stand in front of it, it can decompose most of different molecules.

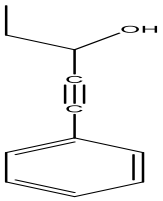
In fact, there are atoms that they need and do not have compounds for them to degrade. As it is mentioned before that candida species need carbon atoms for its different activities [5] so they leave carbon while they destroyed other molecules. Exactly, this looks like a Trojan horse, for the candida from the outside, or in the beginning, it thinks that the carbon atoms are short, or like glucose, in both cases or others it need them and when it enters its cell wall, it will be surprised that it is a long chain of carbon atoms like a saw, which it cannot bear, so its protective wall collapses, leaving it to completely collapse and end, and this is the appropriate and realistic explanation for above activity herbs. This is due to the effectiveness of the above herbs and their carbon molecules figure (9) against the deceptive Candida yeast.

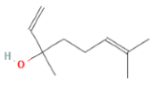
It is true that all the talk is about Candida yeast and the diseases it causes, such as thalassemia, which is our current study, but do not ignoring that fungi or yeasts are similar to bacteria in terms of finding several ways to resist various drugs, and it is remember that when penicillin was discovered, it was quickly resisted, and for this reason below are the compounds that they may become important antibacterial drugs and may be modified to become stronger than they are:











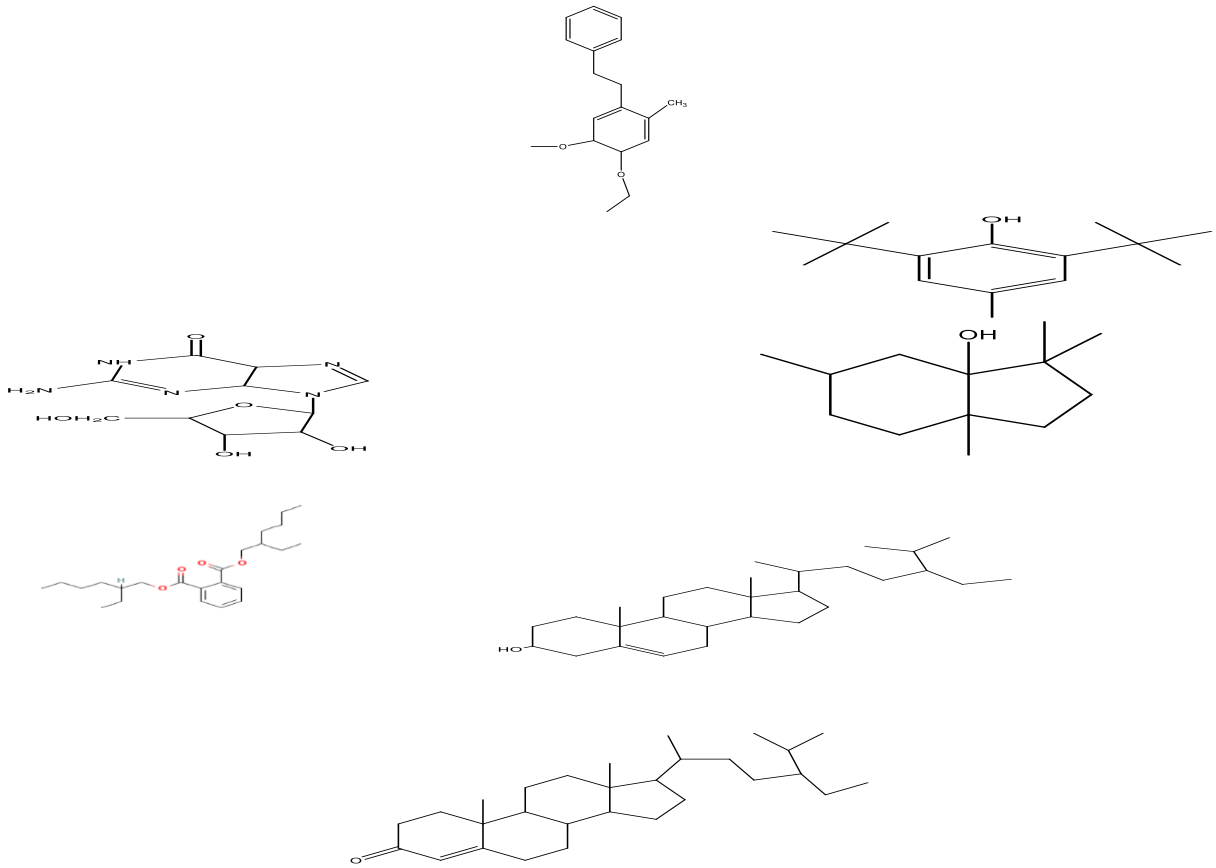


Figure (10): Chemical structures of possible anti-bacterial compounds.

This is so that we have provided various antifungals and various antibacterial, and they can be modified as necessary in order to give the best effectiveness. Thus, these two groups are considered new production lines for medicines that are present and can be used directly without going through a series of procedures because they are materials that were previously used and have been ingested by humans since ancient times.

5- MIC and MFC tests:

Minimum inhibitory concentration (MIC) and Minimum Fungicidal concentration (MFC) were measured to determine the inhibitory concentration and lethal concentration of these effective herbs and compared these results with the drug fluconazole, the results of these are:

Table (8): Results of MIC and MFC for candida.

Concentration µg/ml	1	2	3	4	5	c +	c -
0.5µg/ml	0.37	0.944	0.511	0.675	0.53	0.521	0.167
0.25µg/ml	0.647	0.444	0.387	0.386	0.411	0.549	0.123
0.125µg/ml	0.521	0.485	0.451	0.424	0.407	0.658	0.145
0.0625µg/ml	0.363	0.277	0.761	0.377	0.411	0.494	0.167
0.031µg/ml	0.583	0.324	0.332	0.445	0.565	0.52	0.153
0.015µg/ml	0.342	0.274	0.308	0.256	0.384	0.542	0.112
0.007µg/ml	0.288	0.364	0.343	0.289	0.543	0.564	0.346
0.003µg/ml	0.245	0.314	0.243	0.221	0.575	0.539	0.201
	MIC						
	MFC						

Where; 1= Pomegranate peel in distilled water.
2= Pomegranate peel in acetone 50%.
3= Coriander in boiling water.
4= Cinnamon in boiling water.
5= Fluconazole drug.

Noticing that both solutions of pomegranate peels give more concentrated inhibition and killing values than the drug Fluconazole. While coriander, the third compound, did not give a lethal concentration, but only an inhibitory concentration, and this results may from the large number of different chemical compounds 18 compounds, as it was seen previously. However, the inhibition values of this herb are much lower (0.003µg/ml) than both; other herbs and the drug fluconazole. This leads that compounds of coriander can be used as good treatment for fungal or candida.

Furthermore, from above table (8), that cinnamon herb gave good results, better than the rest of the herbs and the medicine fluconazole in terms of inhibition and killing. But it is difficult to use several different herbs in this study, so this study focused on the herbs pomegranate peel and coriander, which are the herbs that patients take. That is why the above two tests (MIC and MFC) were not done for turmeric, despite its high effectiveness. The reason is that it is difficult to eat in large quantities and is unpalatable. Likewise, cinnamon can be used as making tea, but this study was limited to only two herbs. Firstly, this study was going to use one herb, but it took two herbs, and what happened when giving these herbs to patients was studied.

3. Experimental

The herbal samples were prepared exactly as they have been used by people for a long time and are as follows:

1. Pomegranate peel: add 1 g of this herb in 20 ml 50% ethanol, take the precipitate from each solution and dry them. These precipitate either in ethanol or in water layers so 0.5 g from ethanol's precipitate add to 10 ml 70% acetone with pH=2-2.5. The other one water's precipitate 0.5 g from it add to 50 % acetone.
2. Thyme: 0.5 g from this herb in 10 ml of boiling distilled water. Cool and obtained the product.
3. Lemongrass: 0.5 g from this herb in 10 ml distilled water, boiling for 30 seconds then cooling for preparing the yield.
4. Cinnamon: two of products are made for this herbs; 0.5 g of it to 10 m boiling distilled water, cooling to get the yield. The second is 0.5 g in 10 ml cold distilled water, leave it for 24 hr. to prepare the solution.
5. Coriander: As same as Cinnamon, two products were made for Coriander; 0.5 g in 10 ml boiling distilled water, the other 0.5 g of this herb in 10 ml Acetone for getting the yield.
6. Cumin: 0.5 of this herb to 10 ml boiling distilled water.
7. olive leaf: 0.5 g of this herb in 10 ml of boiling distilled water, continuous boiling was for 20 minutes for obtaining the product's solution.
8. Licorice: 0.5 g of this herb in 10 ml of boiling distilled water, this boiling continues for 15 minutes to get the yield.
9. Garlic: add 0.5 ml of Garlic's oil in 10 ml of distilled water to get the product.
10. Apple vinegar: add 0.5 ml of Garlic's oil in 10 ml of distilled water to obtain the product.
11. add 0.5 ml of Garlic's oil in 10 ml of distilled water to obtain the product.
12. Turmeric: 0.5 g of this herb in 10 ml of distilled water to get the yield.

These procedures were followed in the work of biological activity and in the measurements of GC-MS and also in MIC and MFC.

4. Conclusions

In fact, the field of medicine, especially the field of antifungal and anti-yeast drugs, suffers from a lack of drugs that stand up to these microbes, and perhaps over time these drugs will end, as we saw with the drug Nystatin. Therefore, this field needs to find new drugs continuously, and since we obtained penicillin from fungi, we can use the compounds found in the medicinal herbs that we obtained in this study to kill fungi and bacteria. Thus, this study represents an excellent opportunity to obtain many compounds that can be used as direct drugs because they were basically used previously, so we do not need to measure their toxicity. As we have noticed from the compounds we mentioned in this study, the weak point of fungi, especially Candida yeast, is carbon compounds, especially chains of them.

Therefore, from the above and what we presented in the study, this research provides selected compounds that are strong against fungi and bacteria and can be used medically. Of course, we need other studies in this field because microbial resistance to drugs is ongoing, so studies must continue.

5. Conflicts of interest

There are no conflicts to declare

6. Formatting of funding sources

There is funding sources, the corresponding author responsible for funding.

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8. References and Bibliography

[1] Fisher M. C., Hawkins N.J., Sanglard D. and Gurr S. J. "Worldwide emergence of resistance to antifungal drugs challenges human health and food security" Science 360: 739-742, 2018.

[2] Ferri, M., Ranucci, E., Romagnoli, P., and Giaccone, V. "Antimicrobial resistance: A global emerging threat to public health systems. *Critical Reviews in Food Science and Nutrition*" *57*(13), 2857–2876, 2017. https://doi.org/10.1080/10408398.2015.1077192

[3] Ben Y and et al "Human health risk assessment of antibiotic resistance associated with antibiotic residues in the environment: A review" Envir. Res., 169: 483-493, 2019.

[4] Muteeb G., Rehman M. T., Shahwan M., and Mohammad A. "Origin of Antibiotics and Antibiotic Resistance, and Their Impacts on Drug Development: A Narrative Review" Pharmaceuticals, 16(1615), 2023.

[5] Osagie E. A. and Olalekan S. H. "Multiple Drug Resistance: A Fast-Growing Threat" *Biomed. J. Sci. and Tech. Res. (BJSTR)*, 21(2), 2019.

[6] Saha M and Sakar A. "Review on Multiple Facets of Drug Resistance: A Rising Challenge in the 21st Century*"J of Xenobiotics*, 11: 197-214, 2021.

[7] Fisher, M.C., Alastruey-Izquierdo, A., Berman, J. *et al.* "Tackling the emerging threat of antifungal resistance to human health" *Nat Rev Microbiol* 20: 557–571, 2022. https://doi.org/10.1038/s41579-022-00720-1.

[8] Serwecinska L. "Antimicrobials and Antibiotic-Resistant Bacteria: A Risk to the Environment and to Public Health" *Water*, 12(12): 3313, 2020. https://doi.org/10.3390/w12123313

[9] Dhingra S., Rahman N. A. and et al "Microbial Resistance Movements: An Overview of Global Public Health Threats Posed by Antimicrobial Resistance, and How Best to Counter" Front. Public Health, 8, 535668, 2020. https://doi.org/10.3389/fpubh.2020.535668

[10] Mohi El-Deen* E, Abd El-Gwaad A and Anwar M. M. " Synthesis and Biological Evaluation of Some New Thieno[2,3-b]pyridine-based Compounds As Antimicrobial and Anticancer Agents" Egypt. J. Chem. 66 (2): 231 – 242, 2023.

[11] Mutlaqa D. Z., Al-Shwi* A. A. A. and AbdulJabar L. A. "Antioxidant and Antimicrobial Activities of Some Novel 2-Thiohydantoin Derivatives" Egypt. J. Chem, 64(3): 1315 – 1321, 2021.

[12] Hamdoon A. M., Saleh* M. Y. and Saied S. M. "Synthesis & Biological Evaluation of Novel Series of Benzo[f]indazole Derivatives" Egypt. J. Chem. 65(11): 305-312, 2022.

[13] Duttaa D, Bordoloia* M. J. and Bhattacharyya* N.K "Antimicrobial Compound Isolated from the Plant Pothos scandens L." Egypt. J. Chem., 64 (9): 4803- 4807, 2021.

[14] Vitiello A., Ferrara F and et al "Antifungal Drug Resistance: An Emergent Health Threat" Biomedicines, 11, 1063, 2023.

[15] Mudenda S. "Global Burden of Fungal Infections and Antifungal Resistance from 1961 to 2024: Findings and Future Implications" *Pharmacology and Pharmacy*, 15: 81-112, 2024. 10.4236/pp.2024.154007.

[16] Matins-Santana L., Caroline Patini Rezende, Antonio Rossi, Nilce Maria Martinez-Rossi and Fausto Almeida "Addressing Microbial Resistance Worldwide: Challenges over Controlling Life-Threatening Fungal Infections" *pathogens*, 12(2), 293, 2023; https://doi.org/10.3390/pathogens12020293.

[17] Wafaey* A. A, El-Hawary S, Ismail S, Mohamed S.S, Abdelhameed M. F and Kirollos F. N " Lipid and Essential Oil Profiles of Gliricidia sepium (Jacq.) Kunth. ex. Walp. Leaves and Flowers with Antifungal Effects Against Fluconazole-Resistant Candida albicans" Egypt. J. Chem. 68(6): 27 – 41, 2025.

[18] Boakye-Yiadom E., Odoom A et al "Fungal Infections, Treatment and Antifungal Resistance: The Sub-Saharan African Context" *Therapeutic Advances in Infectious Disease*, 11, 2024 :10.1177/20499361241297525

[19] Lionakis M.S., Drummond R.A. and Hohl T.M "Immune responses to human fungal pathogens and therapeutic prospects" *Nat Rev Immunol*, 23: 433–452, 2023. https://doi.org/10.1038/s41577-022-00826-w

[20] Lockart S.R., Chowdhary A. and Gold J.A. W. "The rapid emergence of antifungal-resistant human-pathogenic fungi" *Nat Rev Microbiol*,21: 818–832, 2023. https://doi.org/10.1038/s41579-023-00960-9

[21] Giannella M, Lanternier F. et al "Invasive fungal disease in the immunocompromised host: changing epidemiology, new antifungal therapies, and management challenges" *Clinical Microbiology and Infection*, 31(1): 29-36, 2025.

[22] Cui X, Wang L. and et al. "Development and research progress of anti-drug resistant fungal drugs" Journal of Infection and public Health, 15(9): 986-1000, 2022.

[23] Garvey M and Rowan N.J. "Pathogenic Drug Resistant Fungi: A Review of Mitigation strategies" Int. J. Mol. Sci., 24(2), 1584, 2023.

[24] Fernandes C.M., Dasilva D and et al. "The future of antifungal drug therapy: Novel compounds and targets" Antimicrobial Agents and Chemotherapy, 65(2), 2021.

[25] Ende M. V, Wijnants S and Dijck P. V "Sugar sensing and signaling in *candida albicans* and *candida glabrata*" Front. Microbiol., 30, 2019.