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RESEARCH ARTICLE
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synthesis and characterization of Pyrimidine from chalcone as a polymeric prodrug with fusidic acid and ZnO and study bioactivity

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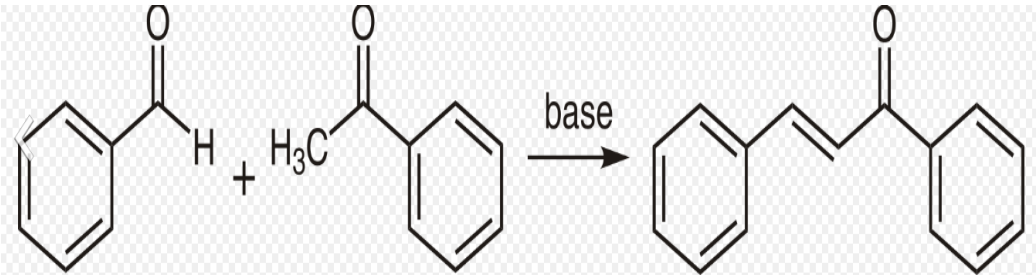
ABSTRACT

Pyrimidine was synthesized as a derivative of chalcone, then polymerization of pyrimidine was carried out with fusidic acid and zinc oxide. All the physical properties affecting the construction process, such as Thin-layer chromatography, solubility, the effect of buffer solutions, and temperatures, were studied. Physical diagnostics such as DSC, TGA, and FT-IR were also studied. The study of the biological activity of the polymer resulting from the interaction of pyrimidine with fusidic acid and zinc oxide, where the study was conducted against three types of bacteria, and the results of the study were compared with the study of fusidic acid alone once and with zinc oxide alone again as a control. The results showed that the process of polymerization of pyrimidine with fusidic acid and zinc oxide gave more effective results against bacteria compared to fusidic acid alone and zinc oxide alone.

Keywords: *chalcone as a polymeric prodrug, Pyrimidine, fusidic acid, ZnO*

INTRODUCTION

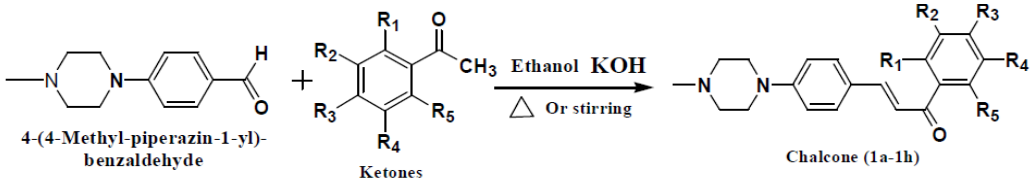
Chalcone (scheme 1) is typically produced by aldol condensation of acetophenone and benzaldehyde. This process, which can be performed without needing a solvent, is so trustworthy that it's frequently utilized in freshman chemistry courses to illustrate green chemistry.



SCHEME 1: simple synthesis of Chalcones

Another name for chalcones is α, β-unsaturated ketones. Chalcones (1,3-diaryl-2-propen-1-ones) are important natural compounds widely present in fruits, vegetables, spices, tea, and soy-based meals. They are thought to be the ancestors of the flavonoid and isoflavonoid families. Open-chain flavonoids called chalcones have two aromatic rings connected by a three-carbon,α, β-unsaturated carbonyl system. Chalcone is a chemical that can be synthesized or found naturally. Due to their usage as starting materials in synthesizing numerous different heterocyclic compounds, chalcones have attracted much attention. Consequently, both organic and medicinal chemists have given the creation of chalcones a great deal of attention (1). O=C-CH=CH (functional group: Scheme 2) is a component that gives chalcones their biological features, such as bacteriostatic/bactericidal action. Chalcones have been the subject of great interest for their exciting and variable pharmacological activities. According to research, chalcones have a wide range of beneficial qualities, including anti-inflammatory, antimicrobial, antifungal, antioxidant, cytotoxic, antitumor, anticancer, cytotoxic, analgesic, antipyretic, antinociceptive, antibacterial, and antileishmanial(2).

Chalcones are regarded as important and valuable syntheses in organic chemistry. According to some reports, chalcones act as building blocks for synthesizing other heterocyclic compounds, acting as precursors for their production. Chromones and their derivatives, such as benzodiazepines, pyrazolines, pyrimidines, isoxazolines, flavones, flavanols, and flavanones, among other molecules, are among the chemicals formed from chalcones (3).



Entry	Product	R_1	R_2	R_3	R_4	R_5
1	1a	H	H	F	H	H
2	1b	H	H	Cl	H	H
3	1c	H	OH	H	H	H
4	1d	H	H	CH_3	H	H
5	1e	H	NO_2	H	H	H
6	1f	H	H	NO_2	H	H
7	1g	Cl	H	Cl	H	H
8	1h	OH	I	H	I	H

SCHEME 2: Synthesis of α, β-unsaturated carbonyl compounds containing 1-Methylpiperazine moiety

clearly, the activity of derivative Chalcone Certain substances have significant antibacterial activity, minimal Staphylococcus aureus inhibitory concentration, and Certain chemicals were more effective against Gram-positive bacteria, especially multidrug-resistant clinical isolates. Chalcones having chloro, bromo, iodo, and hydroxy substitutions at position-2 on A-ring had the strongest anti-diabetic action with glucose medium concentration compared to pioglitazone and rosiglitazone. Hui Zhang tested a number of new chalcone compounds for tubulin inhibition and growth-inhibitory efficacy against MCF-7 and A549 cell lines in vitro (4).

The most important co-active derivatives of Bilogin are pyrimidine, (Fig. 1) is essential for their pharmacological properties. All cells need to the pyrimidines. RNA and DNA are chemical abbreviations. Pyrimidine has a nitrogen atom instead of a carbon atom. Pyrimidines are harder to N-alkylate and N-oxidize than pyridine. Pyrimidines are less basic than pyridine. (5, 6).

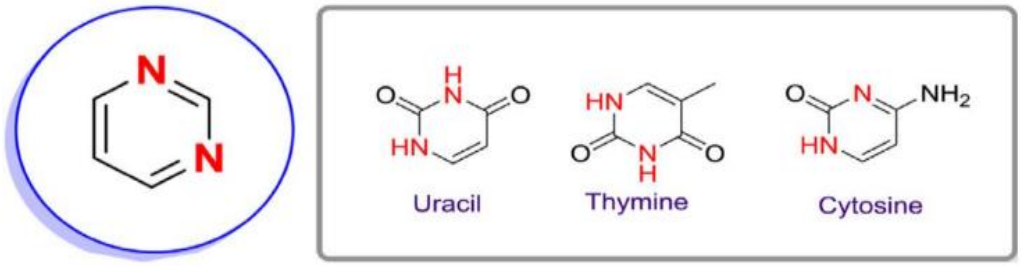


FIGURE 1: Pyrimidine structure, Pyrimidines (uracil, thymine and cytosine) from hydrolysis of nucleic acids.

The fundamental components and three different types of pyrimidine synthesis combine to form the pyrimidine core (Figure 2).

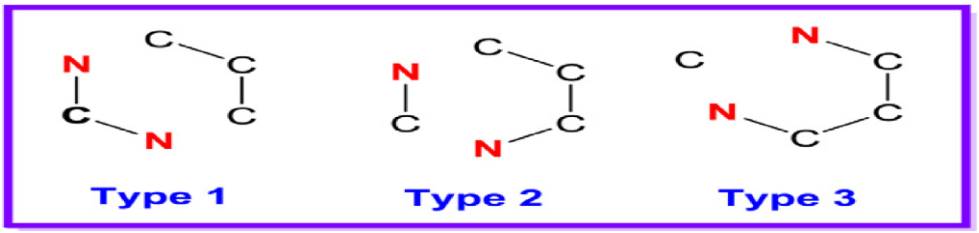
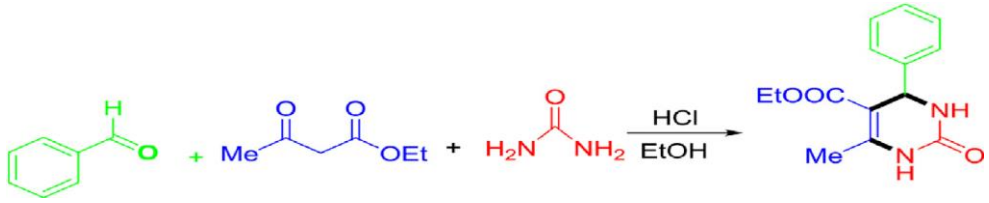
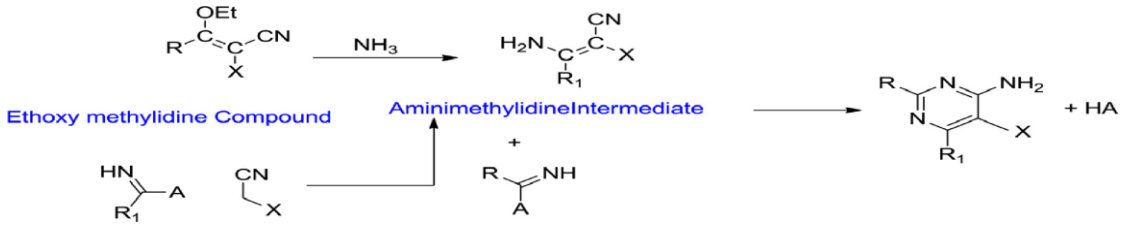


FIGURE 2: Three types of pathways for synthesis of pyrimidines.

Type 1 is more prevalent than Types 2 or 3. This technique enables the production of pyrimidines in a lab setting. The traditional Biginelli reaction is one technique for synthesizing these chemicals organically. In the classic method, ethyl acetoacetate, benzaldehyde, and urea are combined with acid to form the reaction result, 3,4-dihydropyridine-2 (1 H)-one is a solid crystalline substance. Three components make up this reaction (Scheme 4) (7)



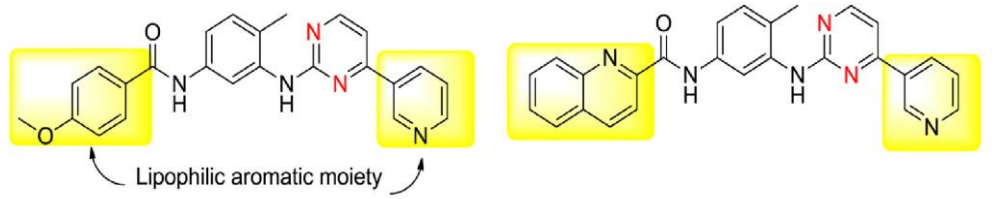
SCHEME 4: Type 1 Biginelli reaction for the synthesis of pyrimidines. The most common variant of type 2 is showed in (Scheme 5).



SCHEME 5: Type 2 pathway for synthesis of pyrimidines

J Popul Ther Clin Pharmacol Vol 30(5):e156–e175; 03 March 2023.

The findings showed that the substance (Figure 3) had strong antifungal activity and had half the efficacy of levofloxacin, a positive control drug, against P. aeruginosa. As anti-microbial and anti-tumor medicines, several compounds of thiazolo[4,5-d], pyrimidine, and dithiazolo[3,2-a:5,4-e]pyrimidinone were studied. The substance was an effective antibacterial agent with little risk of antimicrobial resistance and a high likelihood of effective oral absorption, among other things. Based on high-yielding ultrasonic irradiation techniques, a novel class of methyl thio connected to pyrimidinyl-triazole, oxadiazoles, and thiadiazoles was created. Chloro and nitro-substituted pyrimidinyl-bisthiadiazoles dis- played strong antibacterial activity, according to the link between these compounds' structures and antimicrobial activity (8, 9).



12
% Anti-inflammatory activity at 100 µM= 38.16 %

13
% Anti-inflammatory activity at 100 µM= 86.75 %

FIGURE 3: Structures of benzamide-pyrimidine.

For Pyrimidine antioxidants, the human body is always under assault from oxidative stress, which in turn causes an excessive amount of free radicals to be produced. In particular, the body's reactive oxygen species harm cells, proteins, and deoxyribonucleic acid. Free radicals are linked to the development of a variety of pathological disturbances in people, including aging, cancer, inflammation, atherosclerosis, Alzheimer's disease, and Parkinson's disease. The body's "free radical scavengers," or antioxidants, may lessen oxidative damage and hence lower the risk of chronic illnesses. Pyrimidines are heterocyclic compounds that may be used as antioxidants in medical treatments. Pyrimidine derivatives have recently been employed in creative ways to mitigate the harm caused by the formation of free radicals, and major advancements have been achieved in this area in recent years(10-12).

Clinically used Antioxidants having Pyrimidine Ring, Studies have shown that an increase in free radical generation has a number of harmful impacts on the body. To combat this oxidative stress, the body produces a variety of free radical scavengers. Antioxidants must be replenished from outside the body since the body's defense system becomes less effective with advancing age. Several antioxidants containing pyrimidine nuclei, including riboflavin, thiamine, pyrazolopyrimidine, and triazole pyrimidines, have been created in recent years to achieve this goal (Fig. 4). Despite the abundance of pyrimidine-based antioxidants, only a small number of them are therapeutically employed because of their side effects.(13, 14).

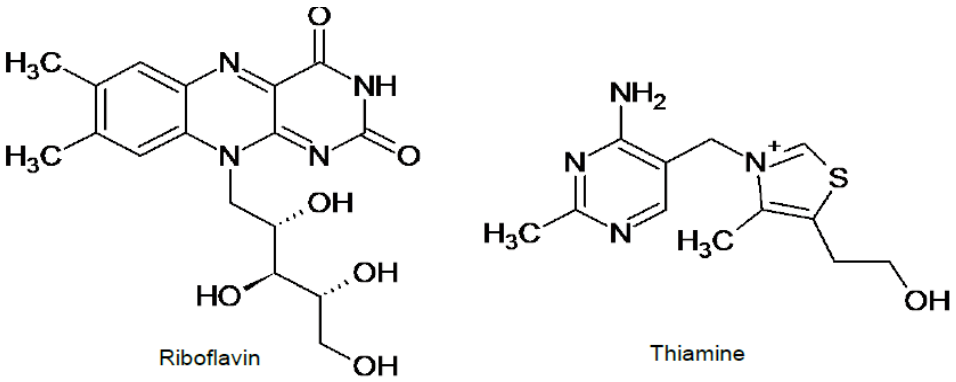


FIGURE 4: Clinically used Antioxidants with Pyrimidine Ring

Fusidic acid (FA) in Figure 5, with a pyrimidine ring as a polymer, plays an important role as an antioxidant, Fusidic acid is an antibiotic that belongs to a group of its own—the fusidate It was obtained from cultures of a fungus, Fusidium coccineum, which was originally isolated from monkey feces. Like several other fungi-produced antibiotics, fusidic acid has an asteroid-like structure but lacks steroid action. The structure is assumed to be in charge of the increased penetration that is steroid-like. One of the most effective antibiotics against S. aureus, Fusidic acid with a pyrimidine ring as antibacterial activity, is targeted precisely at the most prevalent skin infections (15).

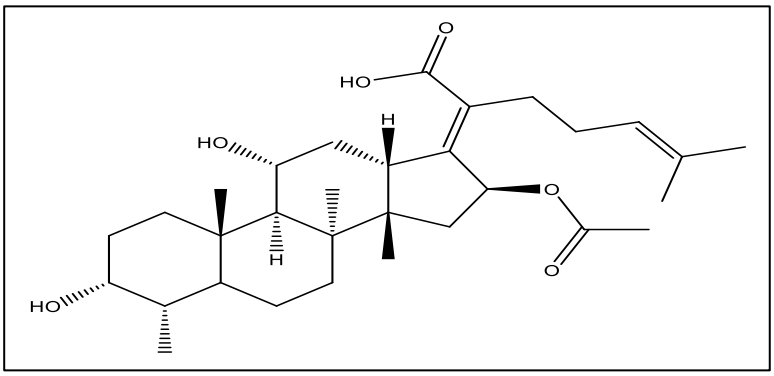


FIGURE 5: Structure of fusidic acid

Fusidic acid (FA) with a pyrimidine ring is a bacteriostatic agent that can be used in a variety of parenteral, topical, and oral formulations to treat infections. The oral and parenteral methods, in contrast, are associated with a number of negative side effects, such as gastrointestinal and liver irritation, hepatotoxicity, diarrhea, phlebitis, and rhabdomyolysis. The systematic distribution and absorption of FA to various body organs have the effect of decreasing its therapeutic potency at the target site. Topical methods are associated with a number of issues, including poor spreadability and skin penetration, local irritability, and inferior potency(16).

Also, Zinc oxide with a pyrimidine ring as a polymer has Antibacterial activity that can start in ZnO-based materials even in the absence of light. Zinc oxide, like other metal oxides, can vary its physicochemical properties in response to environmental factors. However, depending on its concentration, ZnO can be dangerous to the survival of living things and the stability of ecosystems. As a result, considerable consideration is given to how hazardous zinc ions

are released from the solution, particularly in vivo experiments. demonstrated that the toxicity of Zinc oxide with a pyrimidine ring as polymer nanoparticles (ZnO NPs) can be well associated with zinc content and through transformation via the interaction of ZnO with sulfur, phosphate, and ferric oxide. The largest toxicity reduction was seen after phosphating, which can be attributed to phosphates' ability to quickly enclose ZnO NPs and prevent zinc release(17).

Chemicals

The chemical substances that were used in this work are listed in Table 1, along with their suppliers.

TABLE 1: Chemicals and their Suppliers

No	Material	Company
1	polyvinyl pyrolidone	chemcenter
2	Benzyldehyde	Schar-de-hane
3	urea	Toleddo AG
4	Zinc oxide	Himedia-lab
5	Dimethyl formamide	Schar-lab
6	Dimethyl sulphoxide	Alpha chemika
7	Absolute ethanol	Ricdol-de-Hanc/ Germany
8	Chlorophorm	Ricdol-de-Hanc/ Germany
9	DMF	Schar-lab/ Spain
10	HCl 5%	Flucka AG/ Switzorland
11	Methanol	Ricdol-de-Hanc/ Germany
12	NaOH	Himedia-lab/ India
13	KOH	Schar-lab/ Spain
14	DMSO	Alpha chemika/ India
15	Diethyl ether	Schar-lab/ Spain
16	Acetone	Ricdol-de-hane/ Germany
17	SOCl2(Thionyl chloride)	Carl Roth/Germany

synthesis of chalcone

Weight (0.173 gm, 1 mmole) of carboxylated polyvinyl pyrrolidone dissolved in a beaker containing 15 ml absolute ethanol (CH2CH2OH). Heated at 70 oC with a magnetic stirrer, add 5 ml of alcoholic KOH. When adding(0.1gm,1mmole) of benzaldehyde (C6H5CHO), the color changes to yellow after this liquid reflex for 4 hours). With a magnetic stirrer, neutralization with 10 % HCl is done by using a dropper until pH reaches 7. The mixture was filtrated to remove the ppt by using a filtration funnel and filter paper. the solvent evaporated by rotary evaporation for about 6 hours (18).

synthesis of Pyrimidine derivative

Cyclization of alpha, beta-unsaturated ketone with urea (NH2CONH2), Weight (0.261g,1mmole) of Chalcone, and different nucleophile reagents (1mmole of urea, thiourea, and hydrazine) by using sensitive balance. This mixture dissolves in 10 ml of ethanolic sodium hydroxide (C2H7NaO2), 4 gm of NaOH, and 10 ml of ethanol, which is stirred for about 2-3 hours with a magnetic stirrer. This mixture will be poured into a beaker containing 400 ml of cold water and a conscious stirrer for 1 hour. After that, the mixture will be kept in refrigeration for 24 hours. The precipitation obtained will be filtered wash and recyclization mostly by ethanol(19).

Synthesis of polymer prodrugs

The synthesis of the polymer prodrugs was achieved using the following procedures

Synthesis of Pyrimidine Derivatives with Fusidic Acid and ZnO: (0.3g,1mmol) of acid chloride from pyrimidine added to (0.51g,1mmol) of fusidic acid; prepare this solution three times; and (0.3g,1mmol) of pyrimidine added to 20 ml of ZnO solution (1 gm of ZnO in 20 ml of ethanol); prepare this solution three times, separately. cooling (0–5 oC) stirring the reaction mixture for 3 hours for each souluion, then extracting the mixture to remove all adding evaporate. and then washed the dry products with distilled water.

Analytical and Instrumentation techniques

Thermal stability: Newly synthesized compounds (pyrimidine) were heat-diagnosed for the purpose of knowing their thermal stability values.

Thermographic analysis (TGA): The analysis of compounds was performed at the analytical laboratory of Basra University, the College of Science, and the Department of Chemistry, using an SDT Q600 V20.9 build 20 thermogravimeter under nitrogen flow.

Differential scanning calorimeter (DSC) study: The analysis of compounds was performed at the analytical laboratory of Basra University/College of Science/Department of Chemistry, using an SDT Q600 V20.9 build 20 thermogravimeter.

Analytical and spectral techniques

Infrared spectrum: Infrared spectra of the synthesized compounds (pyrimidine) were recorded by an FT-IR 8400S Shimadzu Spectrophotometer (Japan) using a KBr disk in the range 4000-400 cm at the department of pharmaceutical chemistry/college of pharmacy, University of Basrah.

Ultraviolet spectra: The ultraviolet spectra of the synthesized compound (pyrimidine) were recorded by a Cecil 7200 spectrophotometer at the department of pharmaceutical chemistry, college of pharmacy, and University of Basrah.

Thin-layer chromatography: Thin-layer chromatography of the resultant compounds was carried out with the appropriate eluents (ethanol and hexane). UV Tran's illuminators and iodine vapour were used to detect the spots.

Study the effect of solvents on pyrimidine: Prepare 0.005 g of pyrimidine in 10 ml of each solvent (acetone, dichloromethane, chloroform, DMSO, ethanol, and methanol) at room temperature and show the effect of the solvent on the stability of complexes by UV spectroscopy.

Study the effect of solvents on pyrimidine polymer prodrugs: Prepare each Pyrimidine prodrug (0.005 gm of Pyrimidine with 0.005 gm of fusidic acid), (0.005 gm of Pyrimidine with 0.005 gm of ZnO), respectively, in 10 ml of each solvent (acetone, dichloromethane, chloroform, DMSO, ethanol, methanol) at room temperature, and show the effect of the solvent on the stability of complexes by UV spectroscopy.

Study the effect of pH by using a phosphate buffer: Prepare all compounds (0.005 gm of Pyrimidine, thioPyrimidine, and Pyrazoline with 0.005 gm of fusidic acid and 0.005 gm of ZnO, respectively) in ethanol at room temperature and show the effect of pH by UV spectroscopy (20).

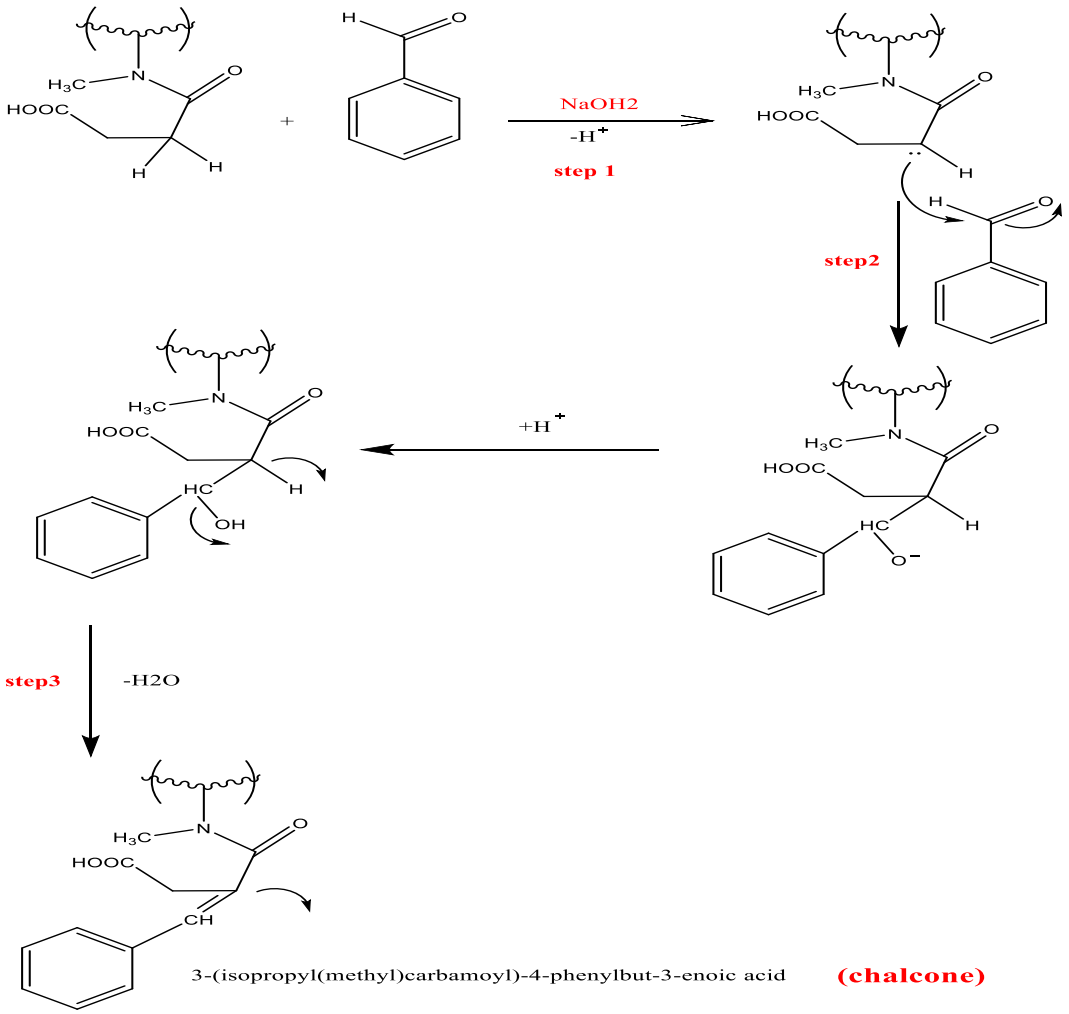
Biological activity

anti Bacterial study of Pyrimidine with fusidic acid: The antibacterial potential of the prepared Samples (Pyrimidine with fusidic acid) was investigated against Gram-negative and Gram-positive bacterial strains using an agar well diffusion assay.

antioxidant study of polymer prodrug: The biological activity effect of polymer prodrugs, Pyrimidine with zinc oxide as antioxidant was studied.

RESULTS AND DISCUSSION

synthesis of Chalcone: Scheme 6 shows the synthesis of a Chalcone.



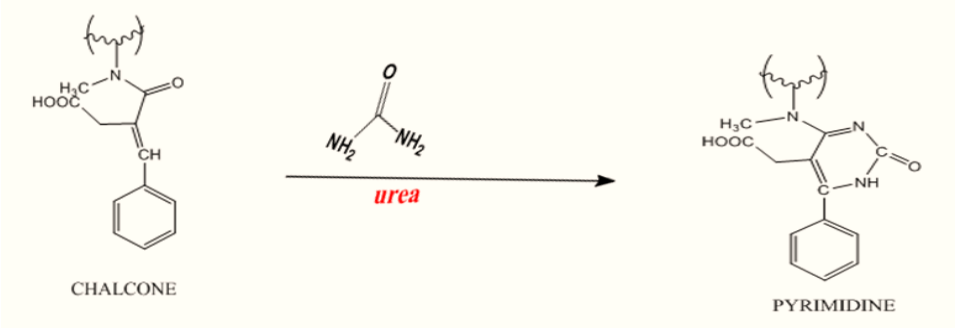
SCHEME 6: Mechanism of synthesis Chalcone

Carbanion or enolate ion production is the first stage of the process. The hydrogen in this ketone will be attacked by the base's hydroxide ion. A generated carbon anion can be stabilized through resonance and release a water molecule. A nucleophilic addition reaction makes up the second reaction step.

When the carbonyl group of the benzaldehyde is attacked by the extra electron in this carbanion or enolate (CH2), a nucleophilic reaction takes place. It produces an alkoxide ion with an excess of electron charge in the O atom.

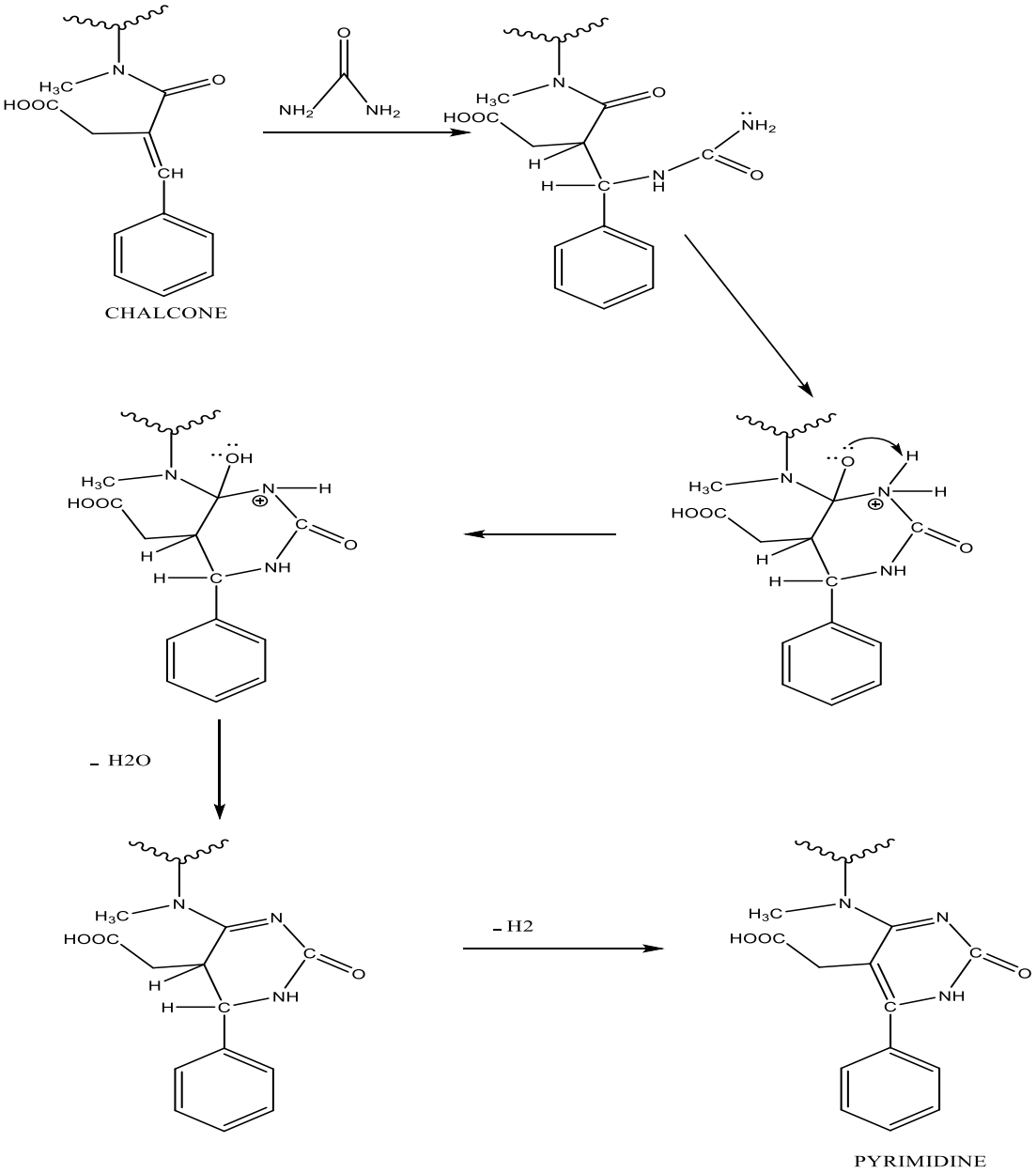
Aldols are created during the fatigued reaction stage. Aldol is a molecule made of aldehydes and ketones that forms B-hydroxyl ketone by absorbing protons from a solvent like water (aldol). The release of water molecules is a phenomenon known as the dehydration reaction. Aldol, which is a carbonyl B-hydroxy, is also easily dehydrated because the compound's double bonds conjugate with the carbonyl group. Aldol compounds that have lost water will produce conjugated, B unsaturated ketones, or chalcone. (21-23).

synthesis of Pyrimidine: Cyclization of alpha, beta unsaturated ketone with (urea NH_2CONH2), Scheme 7 shows the synthesis of a Pyrimidine.



SCHEME 7: synthesis of Pyrimidine

Mechanism of Pyramidine : Scheme 8 shows the Mechanism of a Pyrimidine



SCHEME 8: Mechanism of Pyramidine

J Popul Ther Clin Pharmacol Vol 30(5):e156–e175; 03 March 2023.

Combining a 1,3-dicarbonyl component or chalcone with an N-C-N fragment like urea or an amidine results in the most common synthesis of a pyrimidine ring. In the first reaction stage, the carbon atom in the double bond of the chalcone molecule is attacked by the electrons of "N" in the N-C-N fragment of urea compounds.

In the second step, the intermediate is unstable and this leads to another attack by the second "N" in the N-C-N towards carbon of the carbonyl group which is the nucleophile center. In the third step, the hydrogen will be transferred (H-shifting) to the oxygen alkoxide ion and formed hydroxy pyramiding. The fourth step involves a dehydration reaction and formed pyrimidine (24, 25).

Thermal stability

Differential Scanning Calorimetry (DSC) is one of the thermal decomposition techniques used in studying what happens to the samples to be examined in terms of changes in their condition and thermal transformations resulting from the emission and absorption of heat as a result of the cooling and heating processes. This technique can be applied to many metals and ceramics. And polymers, organic and inorganic materials, pharmaceuticals, and foods by determining their stability and degree of purity. A method for examining how polymers react to heating is differential scanning calorimetry (DSC). DSC can be used to investigate a crystalline polymer's glass transition or melting. A computer and a measurement chamber make up the DSC setup. In the measurement chamber, two pans are heated. The material under investigation is in the sample pan. It is customary to use an empty second pan as a reference. The computer keeps track of the temperature and controls how quickly the pans' temperatures change. A typical heating rate is around 10 ◦C/min(26, 27).

Differential scanning calorimeter (DSC) study

A study of the decomposition of the prepared compounds was carried out using the differential calorimetric decomposition curve (DSC), which showed results shown in the table for the compounds showing the starting temperature (Ti) and the ending temperature (Tf). And the type-whether it emits or absorbs heat—and the shapes of the curves are shown in the table.

The compounds in the DSC were also given decomposition results shown in table 2 and fig 6. Each stage has a type of state, whether it is absorbent or heat-emitting at the maximum temperature, which is consistent with the gravimetric decomposition.

TABLE 2: Thermal Decomposition Results (DSC)

Compound	°C/Ti	Tf/°C	Maximum temperature point°C	Type
Pyramidine	101.037	146.789	119.652	endothermic
	235.370	404.457	328.795	exothermic
	404.457	463.962	457.764	exothermic
	463.962	538.936	499.876	exothermic
	538.936	592.659	577.987	exothermic

Thermographic analysis (TGA)

Thermogravimetric analysis (TGA) of polymers is used to determine weight variations concerning temperature and time. Physical processes, including sublimation, evaporation, and desorption, can also contribute to the weight variations of polymeric materials, such as oxidation and breakdown reactions(28). The study of the relationship between a sample's mass and temperature is known as thermogravimetry (TG). It can be used to research any chemical or physical process that results in a substance losing volatile gases, such as heat deterioration or evaporation. The qualitative "fingerprint" provided by TG in terms of temperature range, extent, and decomposition kinetics gives a quick

way to distinguish one polymer from another using only milligram quantities of material because polymers have varied thermal stabilities29). Table 3 and fig. 7, gives results showing compatibility with the proposed general formula of the ligand and some of its complexes. The table also shows information for each stage of gravimetric decomposition that the complex goes through, as follows:

Ti = temperature at which decomposition begins in one step

Tf = temperature at which decomposition ends in one step

Tmax = maximum weight loss temperature

TABLE 3: Data of the gravimetric pyrolysis curve

Complexe	Step	Ti/°C	Tf/°C	TDTG max	Weight mass loss% found		
Pyramidine		35.762	87.365	47.336	24.0071		
		87.365	296.677	97.774	58.6714		
		296.677	483.385	391.374	17.2857		
Thermal stability of the material at a maximum temperature = 257.685 °C							

In the light of the results of thermogravimetric decomposition of the prepared compounds, it gave thermal stability values of (257.685), for compounds Pyramidine.

The first compound has undergone three stages of decomposition, during which water from crystallization is lost in the first two stages and the material begins to completely decompose at a temperature of 296.677. While the second compound has been given five stages of decomposition, it loses during the first three stages water of crystallization, and during the fourth and fifth stages, the total weight loses to 500.116 and the percentage of loss by practical weight is 100.8494. The third compound has been given three stages of decomposition. In the first two stages, through which water of crystallization is lost, and in the third stage, it begins with the loss of the total substance until it ends at 596.693, A percentage of loss by practical weight was given as 99.904.

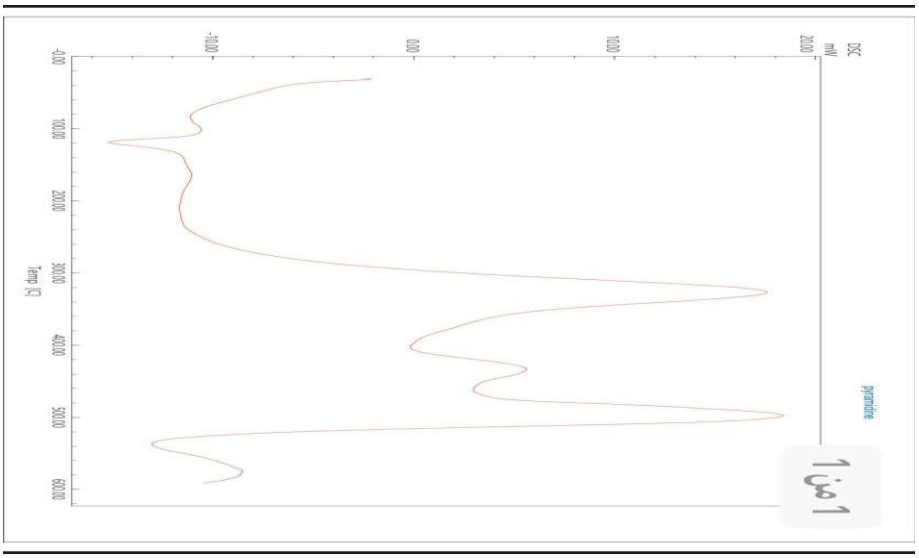


FIGURE 6: DSC of pyrimidine

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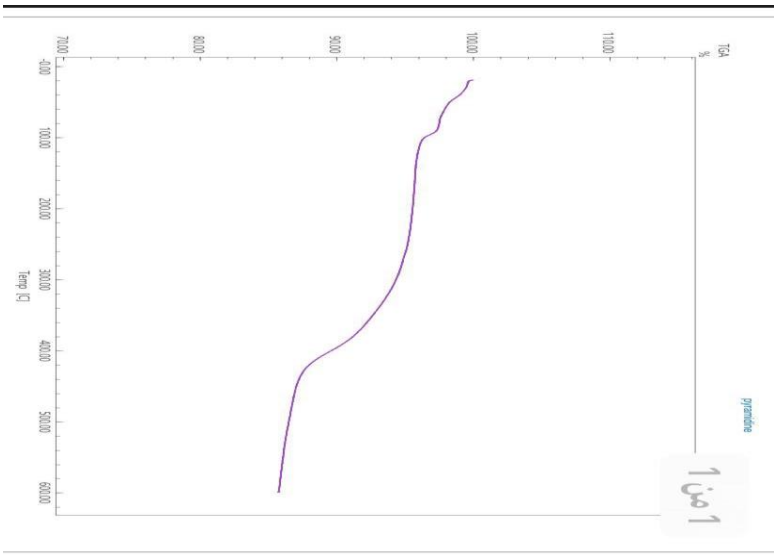

FIGURE 7: TGA of pyrimidine

FT-IR Spectrum of alpha beta unsaturated ketone (chalcone)

Strong absorption band at 1658 cm-1 show in IR spectra table 4, and fig 8, refer to C=O group .medium band show at 1290 cm-1 refer to C-N. weak band show at 2891,2953cm-1 refer to C-H aliphatic. Weak band show at 3064cm-1 refer to C-H of aromatic. The 3000-3175 cm-1 range, which is the defining region for the identification of CH stretching vibrations, must contain CH stretching vibrations in order to be present. In the spectrum of benzene and its derivatives, the ring stretching vibrations, which are a prominent feature of the aromatic ring itself, play a significant role. The, -unsaturated carbonyl group of a chalcone is represented by the conspicuous band between 1625 and 1650 cm1. The C=O stretching mode is characterized by the band in 1658 cm-1(30)

FT-IR Spectrum of Pyrimidine

Strong band show at 3387cm-1 in IR spectra table 4, and fig 9,refer to N-H sec. amine. medium band show at 3180 cm-1 refer to aromatic C-H. weak band show at 1743cm-1 refer to C=O. medium band show at 1608cm-1 refer to C=N. medium band show at 1558 cm-1 refer to aromatic C=C. FT-IR (KBr, cm−1) ν: 3176 (N–H), 2924 (C–H), 1698 (C=N)(31) .

TABLE 4: FT-IR spectra of synthetic compounds

Comp.	C=O	C-N	N-H amines	C-H aliphatic	C-H aromatic	C=N	OTHER
Chalcone.	1656	1290		2953	3064		N-H Amide 3421
Pyrimidine	1743	1292	3387	-	3180	1600	

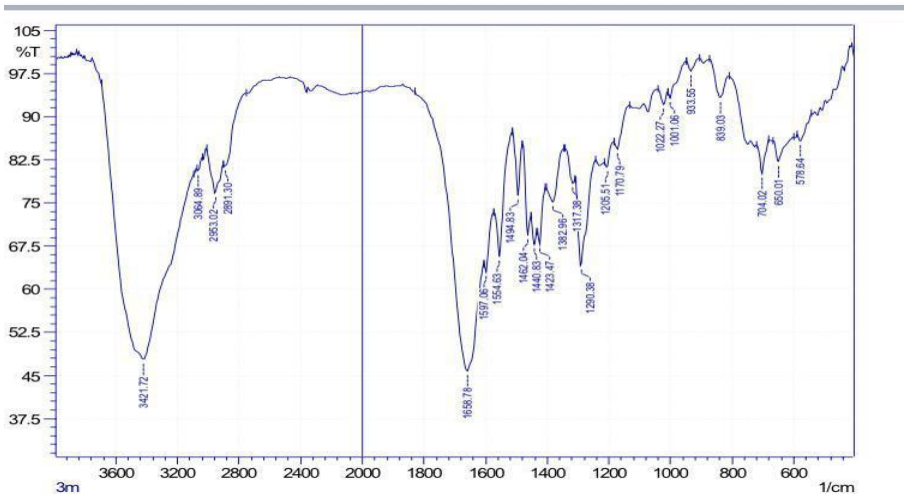

FIGURE 8: FT-IR spectra of chalcone

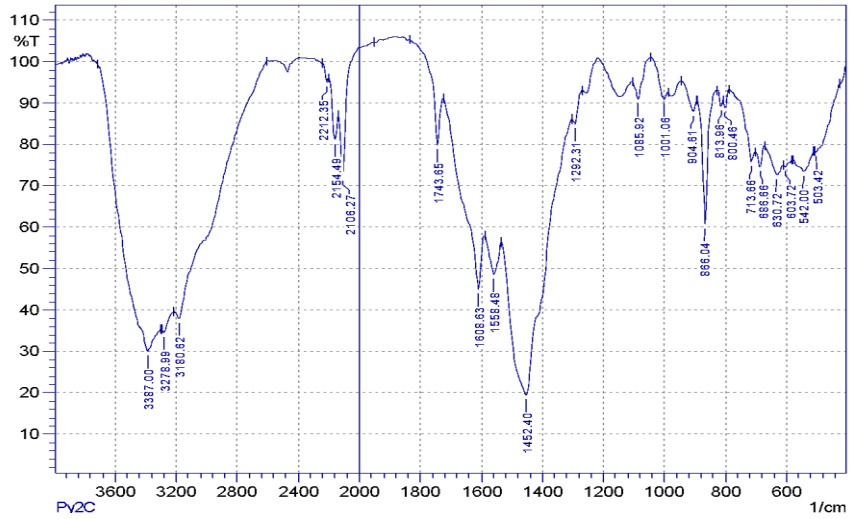

FIGURE 9: FT-IR spectra of pyrimidine

Antimicrobial Effectiveness

Fusidic acid, one of the most significant antibacterial compounds, requires ongoing evaluation of its mechanism of action and rate of resistance to aid in the creation of novel treatment strategies(32). Fusidic acid has a modest antibacterial effect on the majority of gram-positive and gram-negative bacteria at different dosages. (Figs. 10 and 11). Hence, the potential for synergistic effects of the antibiotics pyrimidine against Staphylococcus, Streptococcus, and pseudomonas has been assessed and shown meaningful efficacy at various doses(33). Also, promoting the proper use of this antibiotic in conjunction with other medications is crucial for promoting the prevention of future occurrences of identical spots by emphasizing patient and clinician education (34). as compared to the effectiveness of the several antibiotics that were evaluated. Different antibacterial activities were detected in the outcome(35,36).

The antibiotic (pyrimidine plus fucidic acid) exhibits more antibacterial activity on Streptococcus pyogenes and Staphylococcus aureus than Pseudomonas aeruginosa (Figs. 12 to 14).

On the other hand, this antibiotic was found to have the best activity against Staphylococcus aureus and Streptococcus pyogenes, with a concentration of 200 µg/ml) Our findings show that pyramiding (and this pyramiding plus fusidic acid) exhibited the highest bacterial activity against Pseudomonas aeruginosa (Figs. 13 and 14).

The most important scaffold is pyrazoline, which is used in a variety of pharmaceutical processes. In the cell walls of gram-negative bacteria like Pseudomonas, LDs (Lipopolysacchaxeds) serve as the outer membrane. Low fluidity is provided by hydrocarbon chains in the minor area of LPs. Antibiotics and other organic compounds are extremely effectively blocked from passing through the outer membranes (37). Plasmids, which have the capacity to transmit antibiotic and other antibacterial chemical resistance, are also a part of the genetic composition of Pseudomonas(38). This pyrimidine might cure bacteria due to its extensive action. Its use with other antibiotics may boost its antibacterial effectiveness and prevent topical antibiotic resistance. Intermediate-dose in vitro inhibition has unknown therapeutic consequences. Yet, these effects may help create combinations of drugs that improve therapeutic efficacy and reduce adverse effects (39).

Fucidic acid as control

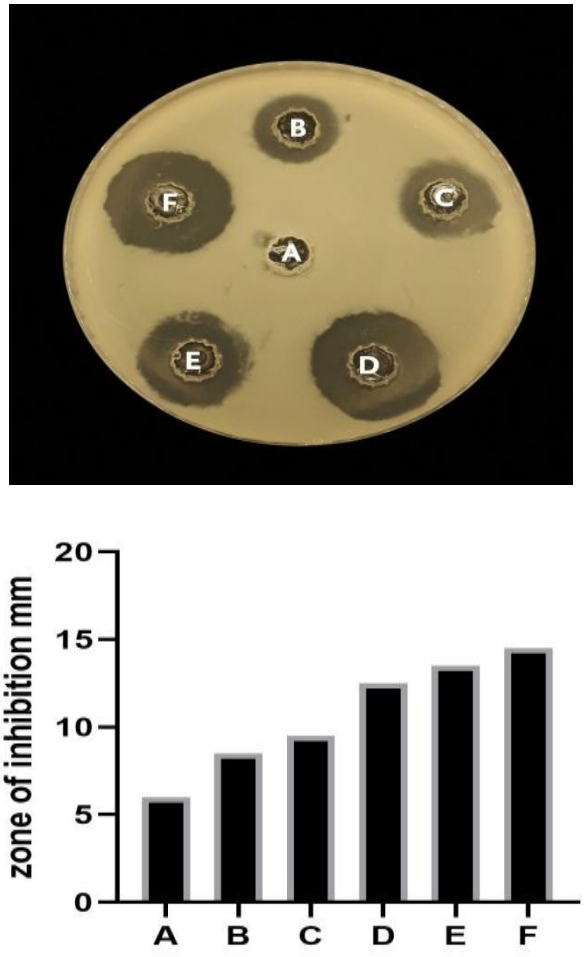

FIGURE 10: Antibacterial activity of (Fu) against Streptococcus. A, control. B, 50 microgram/ml. C, 100 microgram/ml. D, 200 microgram/ml. E, 400 microgram/ml. F,500 microgram/ml .

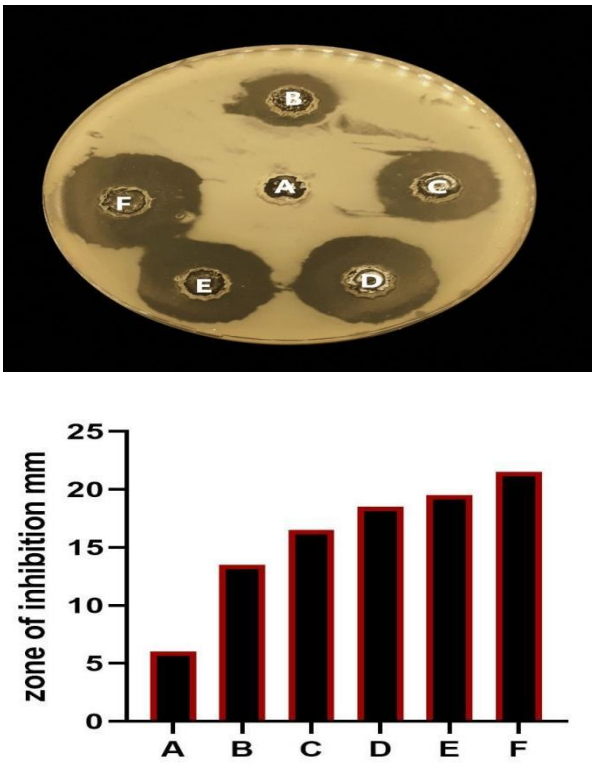

FIGURE 11: Antibacterial activity of (Fu) against Staphylococcus. A, control. B, 50 microgram/ml. C, 100 microgram/ml. D, 200 microgram/ml. E, 400 microgram/ml. F,500 microgram/ml .

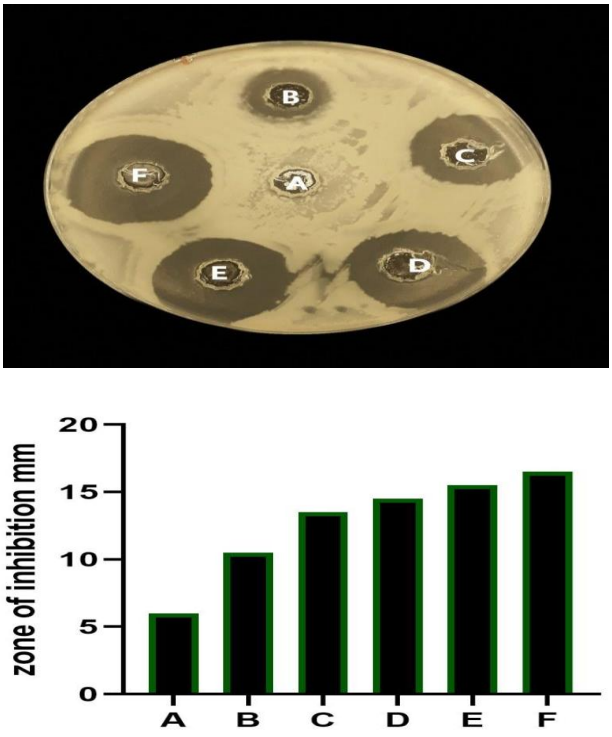

FIGURE 12: Antibacterial activity of (Fu) against Pseudomonas. A, control. B, 50 microgram/ml. C, 100 microgram/ml. D, 200 microgram/ml. E, 400 microgram/ml. F,500 microgram/ml .

J Popul Ther Clin Pharmacol Vol 30(5):e156–e175; 03 March 2023.

Anti-bacterial activity of pyramidine with fucidic acid

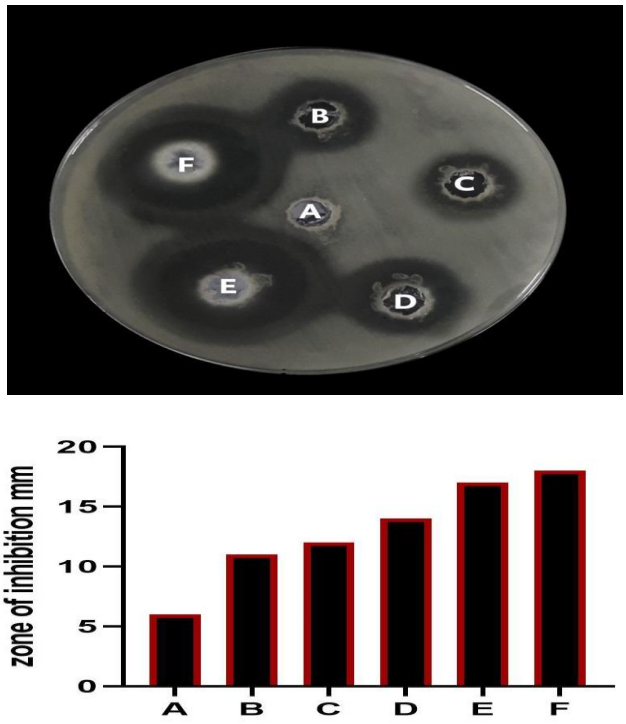

FIGURE 13: Antibacterial activity of (pyramidine plus fucidic acid) against Streptococcus pyogenes. A, control. B, 50 microgram/ml. C, 100 microgram/ml. D, 200 microgram/ml. E, 400 microgram/ml. F, 500 microgram/ml

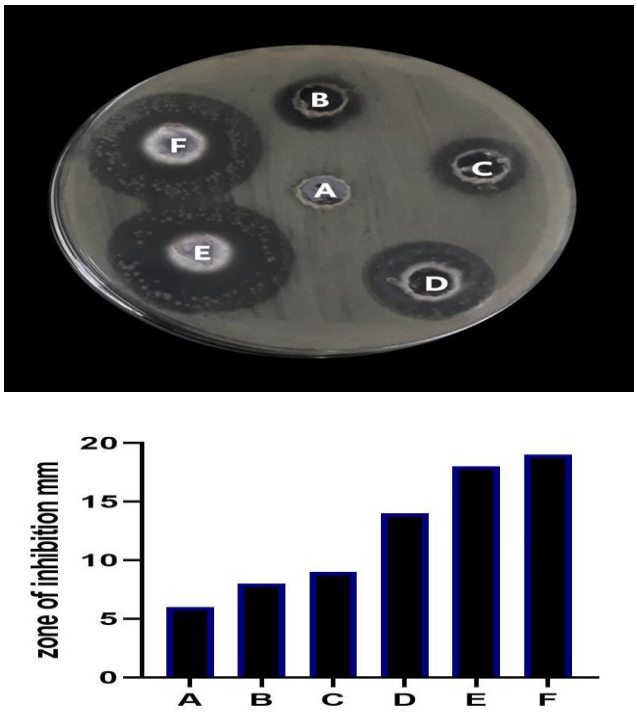

FIGURE 14: Antibacterial activity of (pyramidine plus fucidic acid) against S. aureus A, control. B, 50 microgram/ml. C, 100 microgram/ml. D, 200 microgram/ml. E, 400 microgram/ml. F, 500 microgram/ml

J Popul Ther Clin Pharmacol Vol 30(5):e156–e175; 03 March 2023.

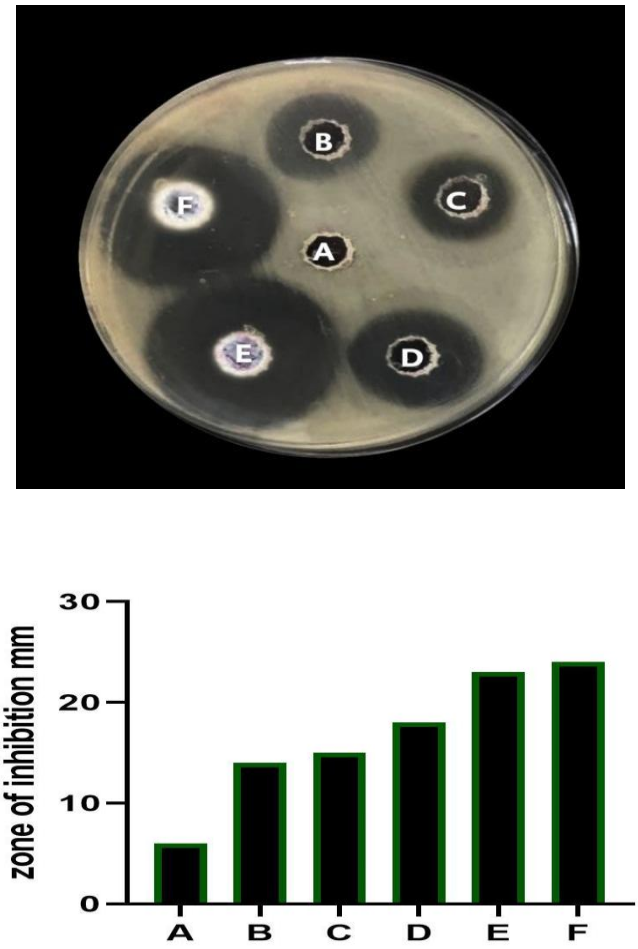

FIGURE 15: Antibacterial activity of (pyramidine plus fucidic acid) against P.aeruginosa. A, control. B, 50 microgram/ml. C, 100 microgram/ml. D, 200 microgram/ml. E, 400 microgram/ml. F, 500 microgram/ml

Antioxidant Performance

Assay For 'Dpph Scavenging

In Figure (16), the scavenging capacity of the (pyrazoline, pyrimidine, and thiopyramidine) was assessed utilizing a steady DPPH (2,2-diphenyl-1-picrylhydrazyl) technique (Sigma–Aldrich, USA) (Sigma– Aldrich, USA). The volume was increased to 2 mL using 100% ethanol after 500 L of DPPH and 500 L of the produced compounds were combined. At 517 nm, the absorbance of each substance was measured(40).

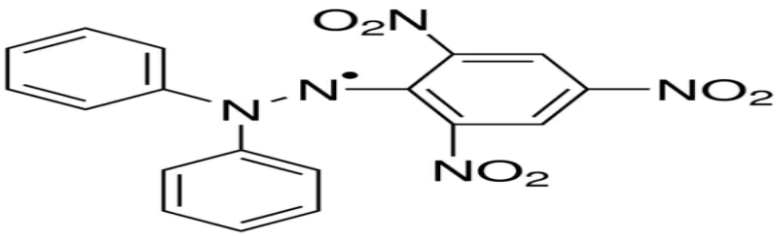

FIGURE 16: Chemical structure of DPPH

J Popul Ther Clin Pharmacol Vol 30(5):e156–e175; 03 March 2023.

Statistical Analysis

The data was statistically analyzed using GraphPad Prism 6(41), which were displayed as the mean and standard deviation of three replicates for each experiment (42,43).

Antioxidant Results

The antioxidant activity of each Zn (fusidic acid), and Zn-1(pyrimidine), was investigated using a DPPH assay. When an electron is spared, DPPH (2,2-diphenyl-1-picrylhydrazyl) has a dependable free radical associated with it. The outcomes are shown in Figure 17. The results demonstrated that the Zn, Zn-1, possess antioxidant action through their capacity to neutralize free radicals. The results are concentration-dependent manner Zinc's capacity to slow down oxidative processes has been acknowledged and researched. Zn's antioxidation mechanism can generally be split into acute and long-term effects. Chronic effects are caused when a biological system is exposed to zinc over an extended period of time, which induces the production of another chemical that is the ultimate antioxidant, such as metallothioneins. Prolonged zinc deficiency typically increases vulnerability to several forms of oxidative stress Two mechanisms contribute to the acute effects: either protein sulfhydryls are protected, or z OH production from H2O2 is reduced due to the antagonistic action of redox-active transition. metals like iron and copper (43). One of three processes is hypothesized to reduce sulfhydryl reactivity in order to protect protein sulfhydryl groups: zinc's direct interaction with the sulfhydryl, attaching to a different protein location adjacent to the sulfhydryl group causes steric hindrance or a conformational change as a result of interaction to another protein location (44, 45).

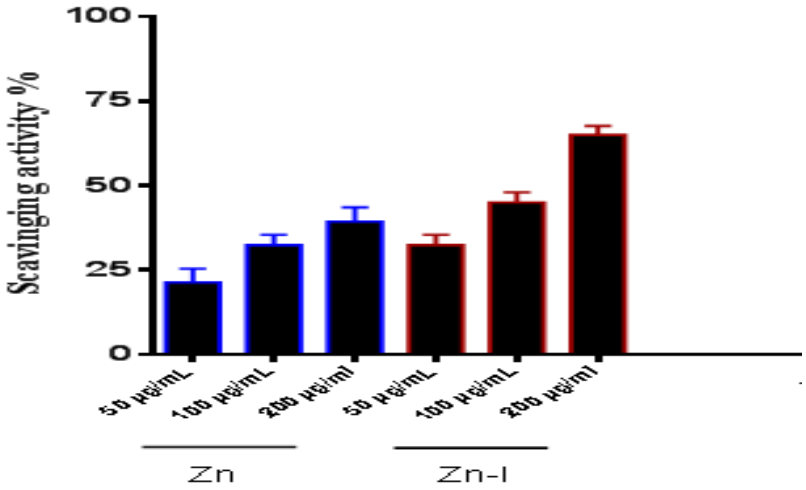

FIGURE 17: Activity against free radicals in Zn and its compounds. The results are shown as mean standard deviation.

CONCLUSION

Synthesis of polymer prodrug and testing its activity as an antibacterial against different strains of bacteria for topical preparation. Synthesis of polymer prodrug and testing its activity as an antioxidant for topical preparation. Some prepared polymer prodrugs exhibited medium to good antibacterial activity against Pseudomonas aeruginosa, staphylococcus aureus, and streptococcus pyogenes when compared with the parent agent. All prepared polymer prodrugs exhibited good antioxidant activity when compared with the parent agent.

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