



“Synthesis, Characterization of Novel, potent Azetidinone’s Derivatives and Their Utilisation as Antifungal Activity”

Sanjeev Kumar Bhatt^{1*}, Indu Singh¹, Sanjay Vats,
Bhopal Singh¹ Gourav Kumar,

ABSTRACT:

3-chloro-4-(substitutedphenyl)-1-(5,5,7-trimethyl-3a,4,5,6,7,7a-hexahydrobenzo[d]thiazol-2-yl) azetidin-2-one 3(a-d) and 2(a-d) were prepared by systematic route. Compound (1) 5,5,7-trimethyl-3a,4,5,6,7,7a-hexahydrobenzo [d] thiazol-2-amine was prepared by reaction between 5,5,7 tri methyl cyclohexanone reagent (AR. Grade Aldrich) batch 2020 and with thiourea. Compounds 2(a- d) N Substituted benzylidene 5, 5, 7 tri methyl 3a, 4, 5, 6, 7,7a hexahydrobenzo (d) thiazol- 2 amine) were prepared from (1) compound and different derivatives of aromatic aldehyde, then compounds 3(a-d) were synthesis from derivatives of 2(a-d). Synthesis of compounds 3(a-d) showed better valuable characteristic and efficacy as antifungal. In these compounds chloro and hydroxyl azetidinone derivatives showed better inhibition nature as compared to standard drugs and less side effect. Other derivatives of azetidinone also showed the proper affectivity. A new class of 3(a-d) series of azetidinone nucleuses possess better biological property (antifungal properties) and in medicinal chemistry. The structure of new synthesised compounds was identify and confirmed elemental analysis by, IR, NMR, and their properties were screened as antifungal activity. Purity of synthesised derivatives of azetidinone was checked with the help of TLC.

Key words: Azetidinone, antifungal activity, thiazoles, fluconazole.

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INTRODUCTION:

Now a day’s number of life are treating infection caused by fungal disease. Azetidinones are useful structural requirement in the field of medicinal chemistry. Azetidinone drug derivatives exhibit different biological activity like antimicrobial^{1,2} antibacterial³ antifungal⁴⁻⁶. Benzothiazol derivatives have also shown diverse biological activities such as antimicrobial⁷ and antifungal⁸, antibacterial⁹⁻

¹⁰. In antifungal effect against aspergillus species¹¹, some novel compound of azetidinone uses as antifungal and anticonvulsant¹²⁻¹³ activities and affectivity of azetidinone¹⁴ showed antifungal property Azetidinone derivatives of Schiff base also function as depressant agent¹⁵, bacterial agent¹⁶ and antimicrobial¹⁷ biological application¹⁸⁻²⁷ agents. Small ring heterocyclic azetidinone and thiazolidinone

derivatives containing nitrogen, sulphur and oxygen showed good medicinal properties in biological system; however older drug derivatives show high frequency of renal toxicity and several side effects. In this

Chemistry:

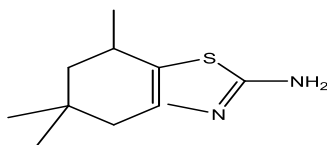
3-chloro-4-(substitutedphenyl)-1-(5,5,7-trimethyl-3a,4,5,6,7,7a-hexahydrobenzo[d]thiazol-2-yl) azetidin-2-one 3(a-d) and 2(a-d) were prepared by systematic route. Compound (1) 5,5,7-trimethyl-3a,4,5,6,7,7a-hexahydrobenzo [d] thiazol-2-amine was prepared by reaction between 5,5,7 tri methyl cyclohexanone reagent (AR. Grade Aldrich) batch 2020 and thiourea. Compounds 2(a- d) N Substituted benzylidene 5, 5, 7 tri methyl 3a, 4, 5, 6, 7,7a hexahydrobenzo (d) thiazol- 2 amine) were prepared from (1) compound and different derivatives of aromatic aldehyde then compounds 3(a-d) were prepared from derivatives of 2(a-d). Synthesis of compounds 3(a-d) showed better valuable

MATERIAL AND METHOD:

In this work different reagents (AR grade) were used and dissolved in proper solvents. Reaction procedure and Completion were performed at different condition. Melting points were noted down by m.p. apparatus using ordinary glass capillary tube. The homogeneity of all newly synthesized derivatives, and purity of Reaction recorded

EXPERIMENTAL:

1: Synthesis of 5, 5, 7-trimethyl-3a, 4, 5, 6, 7, 7a-hexahydrobenzo [d] thiazol-2-amine (1)



research work, we have synthesised some novel potentially drug derivatives 3(a –d) which have shown the better antifungal activity with less side effects.

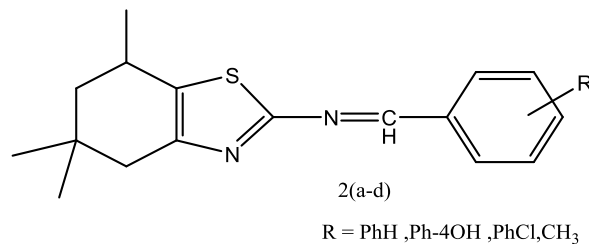
characteristic and efficacy as antifungal. In these compounds chloro and hydroxyl azetidinone derivatives showed better inhibition nature as compared to standard drugs and fewer side effects. Other derivatives of azetidinone also showed the proper affectivity. A new class of 3(a-d) series of azetidinone nucleuses possess better biological property (antifungal properties) and in medicinal chemistry. The structure of new synthesised compounds was identify and confirmed elemental analysis by, IR, NMR, and their properties were screened as antifungal activity. Purity of synthesised derivatives of azetidinone was checked with the help of TLC.

by (TLC) plate method on silica gel. Perkin Erlmer 2400 was used to confirm different portion of elemental part. Beckman spectrometer and Brucker (300) DPX were used to check different values of IR (cm⁻¹ max.) and ¹H NMR (in CDCl₃ solvent) respectively).

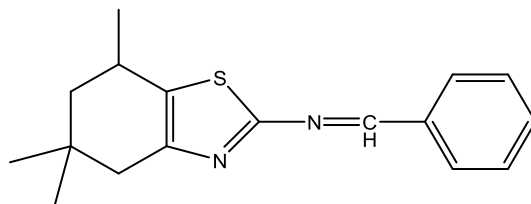
Take a reagent 5,5,7 tri methyl cyclohexanone (2.8 gm, 0.02 mol) with ethyl alcohol (18 ml) in round bottom flask and added thiourea (3.04g , 0.04mol),solid iodine (5.07 gm , 0.02 mol). This mixture was mixed properly through stirring. It was heated and refluxed at right temperature about 6 hour. Progress of the reaction was checked through TLC timely. Sample was taken in beaker and one drop of ammonia solution was added. When crystals were formed, stop the refluxing and cool down at room temperature. It was again cool down to decrease 20 ° C in 200 ml of water. This solution was basified with liquor ammonia through adding one or two drops in solution

(RBF). It was put aside to crystallization, after crystallization, crystal was extracted through ethyl acetate (CH₃COOC₂H₅) (105ml) and crude crystal was purified through column chromatography using chloroform as fluent and silica gel (70- 230 mesh) as solid phase. The pure form of crystals was formed with pale white solid. Yield of the compound 73 %, MP 55-57 °C, KBR v_{max} cm⁻¹) IR: 3455 (NH₂), 3040(C, H ring), 2953 (CH₃), 2870 (CH₂ m), 1562 (C=N), 758 C-S-) and NMR values as (CDCl₃ + DMSO-d₆) δ in ppm: 0.94 (s 2x3H, CH₃), 0.86 (s 1x3H, CH₃), 1.48-2.95 2x2H(s, CH₂),2.1 ,1x1H(-CH) ,9.14 ,1x1H (s , NH₂)

2: General Procedure of Synthesis of N Substituted benzylidene 5, 5, 7 tri methyl 3a, 4, 5, 6, 7,7a hexahydro benzo (d) thiazole-2 amine 2 (a - d) :



Compound 2a :



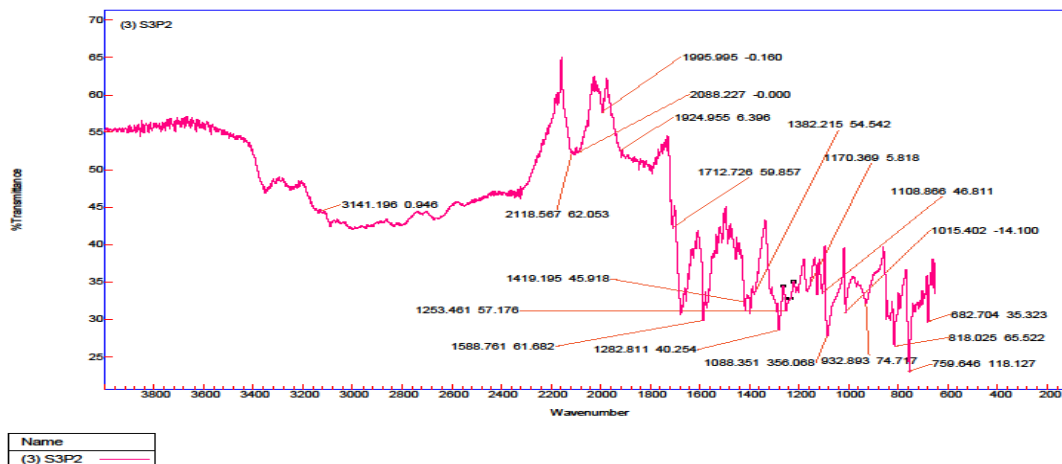
Take a solution of compound 1 (1.96 g, 01 mol) with benzene (30 ml) in RBF and added substituted benzaldehyde (1.12g, 0.01 mol) presence of 5 ml acetic acid. It was refluxed for 3.30 hour in dean Starks apparatus in which water is remove azeobatically. Completion of reactions was checked with the help of TLC plate. In

mixture portion eluent was used as ethyl acetate and toluene in 1:4 ratio. When the reactions were completed the reaction solution of refluxing stop and remove the solvent by distillation and solid compounds were achieved then it was filtered, washed and re-crystallized by ethanol to obtained pure compounds 2a with light pale colour,

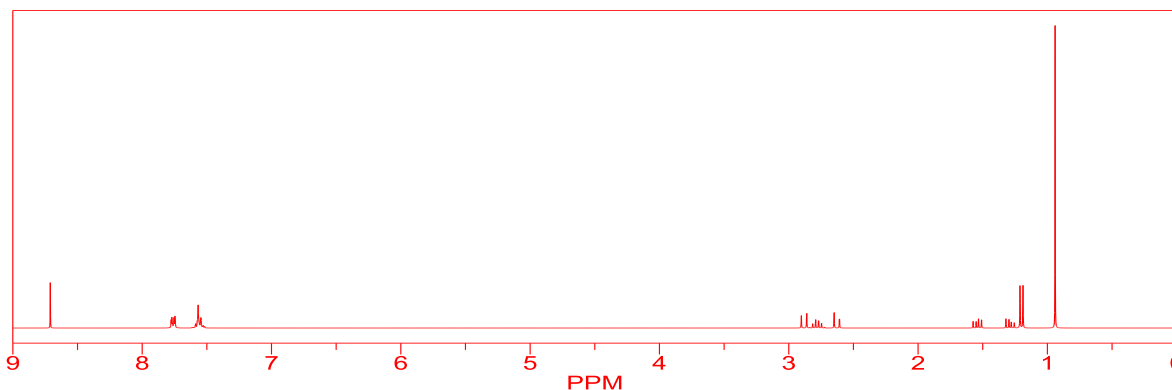
IR: (KBr , ν_{\max} , cm^{-1}): 786 (C-S-C), 1301 (C-N), 1510 (C-C, Ar ring), 1565 (C=N), 3042 (C-H ring), $^1\text{H NMR}$: (DMSO- d_6 + CDCl_3) values of δ in ppm: 0.94 (s, 2 \times 3H,

CH_3), 1.20 (d , 1 \times 3H , CH_3) , 1.54 (d , 1 \times 2H , CH_2) , 2.88 (s , 1 \times 2H , CH_2) , 2.78 (m, 1 \times 1H , CH) , 8.71(s, 1 \times 1H , CH-N) , 7.55-7.71(s , 5 \times 1H , CH-Ar ') ,

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2a: 1-phenyl-N-(5,5,7-trimethyl-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)methanimine

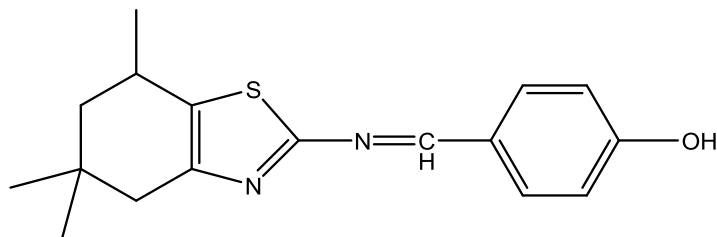


2a : 1-phenyl-N-(5,5,7-trimethyl-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)methanimine

The following compounds (2b-2d) were prepared using a similar procedure described to compound 2a. The physical, spectral data

(values) of derivatives 2b-2d was given in table 1 and below respectively.

2b: Infra red data 4-(((5,5,7-trimethyl-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)imino)methyl) phenol :

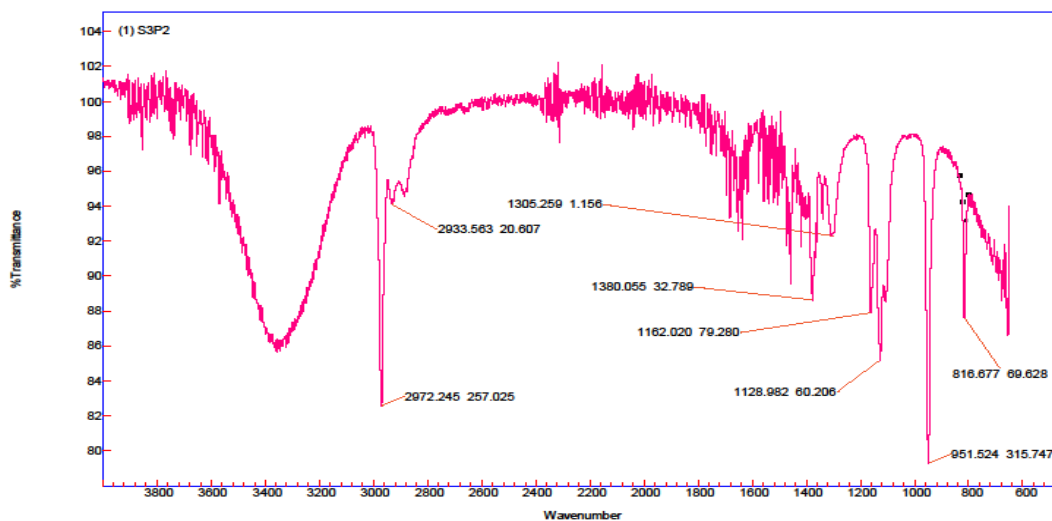


IR (ν_{\max} cm^{-1} , KBr): 786 (C-S-C), 1301 (C-N), 1510 (C-C Ar. ring), 1565 (C=N-), 3040 (C-H ring), 3420 (-O-H Ar), 1060 (C-O), ^1H NMR (CDCl_3 + DMSO-d_6) δ data in ppm: 0.93(s, $2 \times 3\text{H}, \text{CH}_3$), 1.20(d, $1 \times 3\text{H}$

, CH_3), 1.54(d, $1 \times 2\text{H}, \text{CH}_2$), 2.88(s, $1 \times 2\text{H}, \text{CH}_2$), 1.54(m, $1 \times 1\text{H}, \text{CH}$), 8.71(s, $1 \times 1\text{H}, \text{CH-N}$), 7.54-771(s, $4 \times 1\text{H}, \text{CH-Ar}$), 9.68(s, $1 \times 1\text{H}, \text{OH-Ar}$),

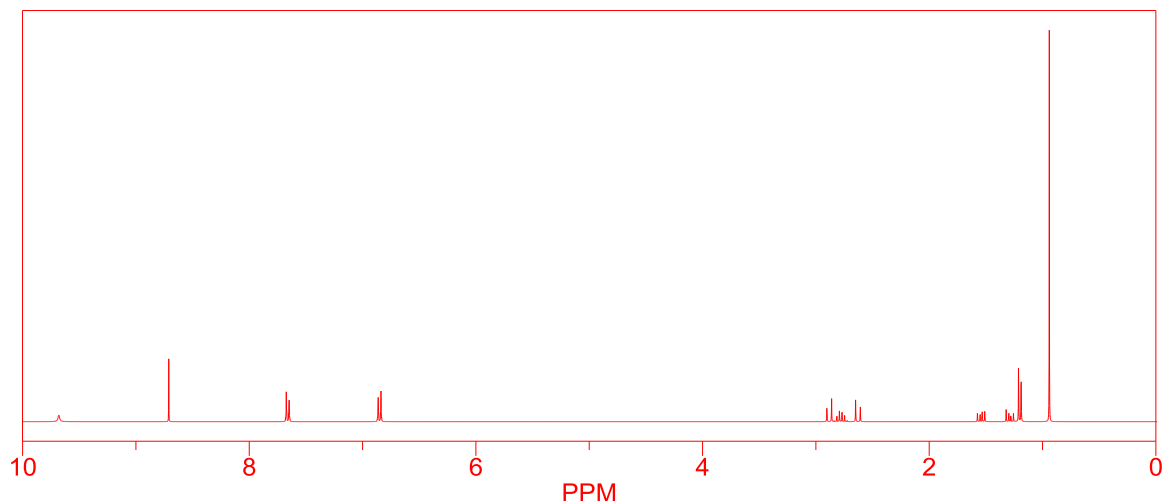
2c: 1-(4-chlorophenyl)-N-(5,5,7-trimethyl-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)methanimine

Agilent Resolutions Pro



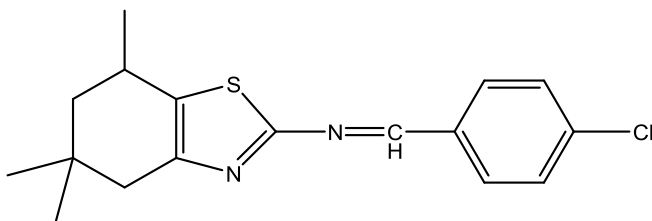
Name
(1) S3P2

2 b : 4-(((5,5,7-trimethyl-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)imino)methyl)phenol :



2 b : 4-(((5,5,7-trimethyl-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)imino)methyl)phenol

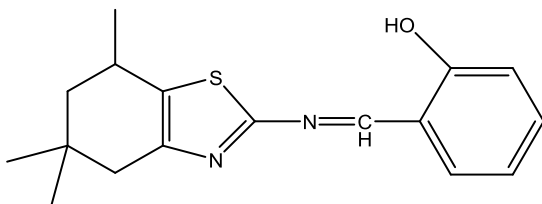
2c: 1-(4-chlorophenyl)-N-(5,5,7-trimethyl-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)methanimine :



IR (KBr ν_{\max} cm^{-1}): 786 (C-S-C-), 1301 (C-N-), 1510 (C-C of Ar ring), 1565 (-C=N), 3042 (C-H ring), 750 (C-Cl) $^1\text{H NMR}$ (DMSO- d_6 + CDCl_3) δ values in ppm: 0.94(s, $2 \times 3\text{H}, \text{CH}_3$), 1.21(d, $1 \times 3\text{H}, \text{CH}_3$), 1.54(d

, $1 \times 2\text{H}, \text{CH}_2$), 2.88(s, $1 \times 2\text{H}, \text{CH}_2$), 1.54(m, $1 \times 1\text{H}, \text{CH}$), 8.71(s, $1 \times 1\text{H}, \text{CH-N}$), 7.54-771(s, $4 \times 1\text{H}, \text{CH-Ar}$).

2d: 2-(((5,5,7-trimethyl-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)imino)methyl)phenol :

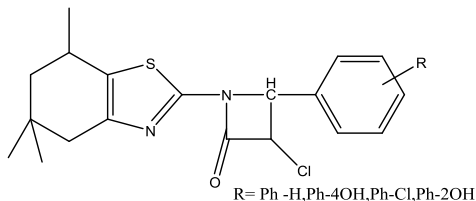


IR (ν_{\max} cm^{-1} , KBr): 786 (-C-S-C-), 1301 (-C-N), 1510 (C-C Ar ring), 1565 (C=N), 3042 (C-H ring), 3400 (-O-H Ar), 1061 (C-O) $^1\text{H NMR}$ (CDCl_3 + DMSO- d_6) δ in ppm: :

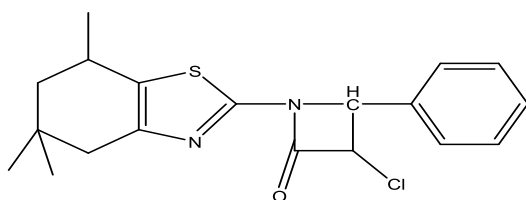
0.94(s, $2 \times 3\text{H}, \text{CH}_3$), 1.20(d, $1 \times 3\text{H}, \text{CH}_3$), 1.54(d, $1 \times 2\text{H}, \text{CH}_2$), 2.88(s, $1 \times 2\text{H}, \text{CH}_2$), 1.54(m, $1 \times 1\text{H}, \text{CH}$), 8.71(s, $1 \times 1\text{H}, \text{CH-N}$),

6.93-771(s ,4×1H ,CH- Ar) , 11.11(s ,1×1H ,OH- Ar) ,

3: General process of synthesis of 3-chloro-4-(Substituted phenyl)-1-(5, 5, 7-trimethyl-3a, 4, 5, 6, 7, 7a-hexahydrobenzo[d]thiazol-2-yl) azetidin-2-one 3(a-d)

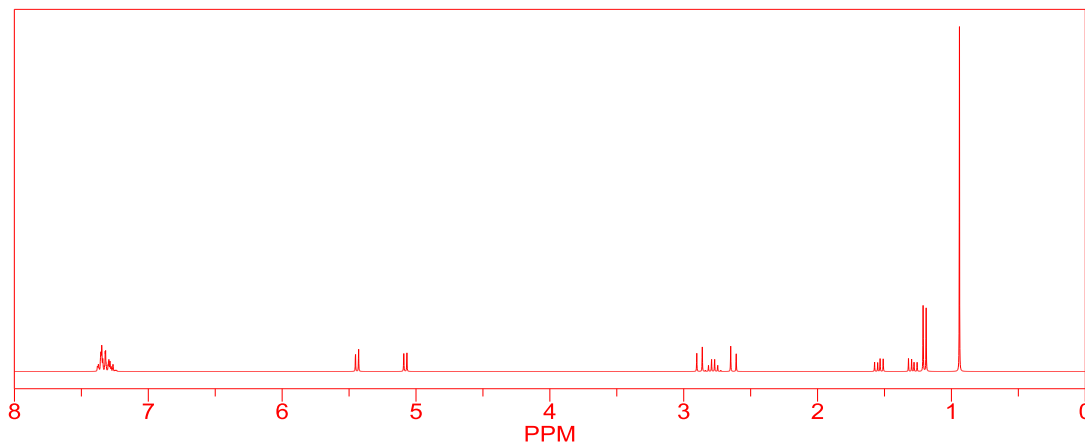


3a : 3-chloro-4-phenyl-1-(5,5,7-trimethyl-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)azetidin-2-one



Take the compound 2a (0.01mol) of Schiff base in 1,4 dioxan (30 ml) and tri ethyl amine (0.01 mol) and cool down the solution 0 to 5⁰C temperature then added chloro acetyl chloride (0.02 mol) drop by drop with constant shaking. This reaction mixture was refluxed 4 - 6 hr and progress of reaction was checked with the help of TLC. Excess solvent separated through distilled off then resulting mixture part was poured into crushed ice water and put it for formation of crystal at overnight. The crystals were formed filtered, washed, and

dried. The synthesized compound was purified with the help of column chromatography through silica gel (70-230 mesh). In it, eluent was used as chloroform and n hexane in ratio 40:60. IR (KBr ν_{max} cm^{-1}) : 750 (CH-Cl), 786 (-S-C), 1301 (C-N), 1510 (-C-C- Ar ring), 1565 (-C = N), 3042 (C-H ring), 1735 (C=O), ¹HNMR (CDCl₃, DMSO-d₆) ppm (δ): 0.94(s, 2×3H,CH₃),1.20 (d ,1×3H ,CH₃),1.54(d ,1×2H ,CH₂), 2.88(s ,1×2H ,CH₂), 5.08(d,1×1H ,NCH), 5.44(d,1×1H ,N- CH Cl), 7.27-7.36(s ,5×1H ,CH- Ar)

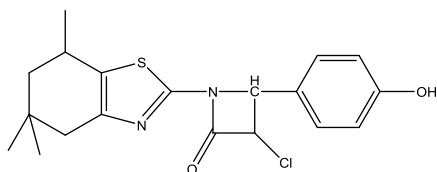


3-chloro-4-phenyl-1-(5,5,7-trimethyl-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)azetidin-2-one,

The following compounds (3b-3d) were prepared using a similar procedure described to compound 3a. The physical, spectral data

record of compounds 3b-3d are giving in table 1 and below respectively.

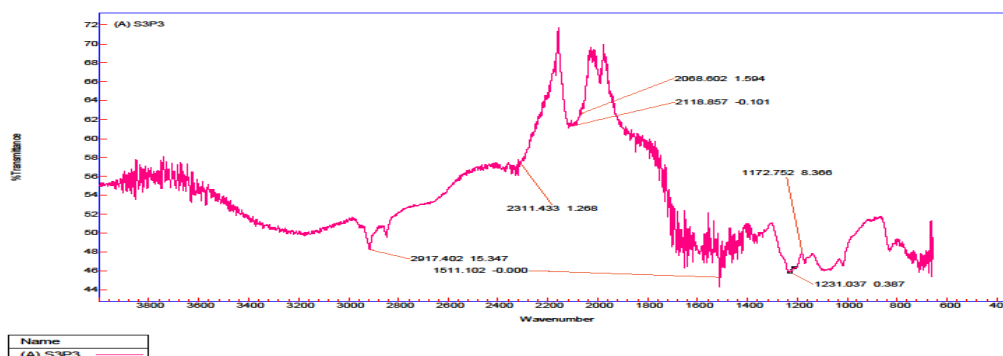
3b: 3-chloro-4-(4-hydroxyphenyl)-1-(5,5,7-trimethyl-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)azetidin-2-one



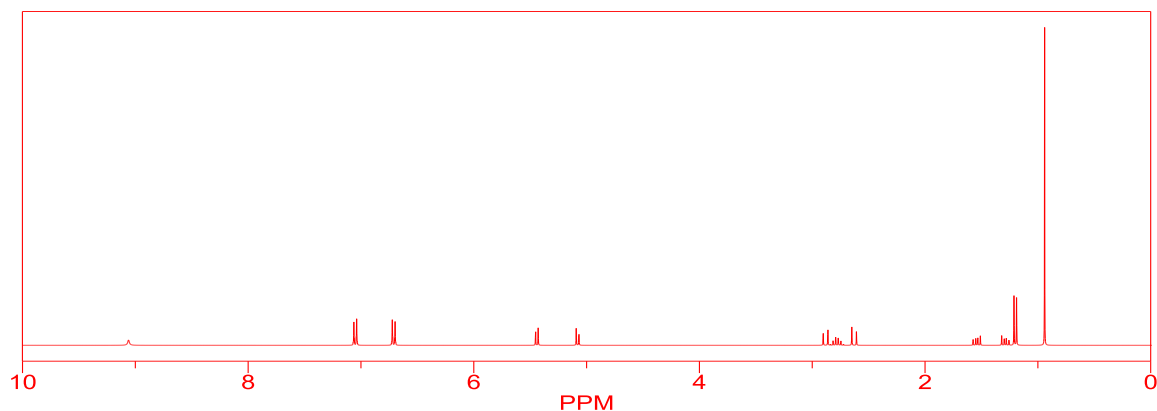
IR (KBr $\nu_{\max} = \text{cm}^{-1}$) : 750 (CH-Cl), 786 (-S-C), 1301 (C-N), 1510 (-C-C- ar ring), 1565 (-C = N), 3042 (C-H ring), 1736 (C=O) , 3440 (O-H Ar), 1057 (C-O) $^1\text{HNMR}$ (CDCl₃ , DMSO-d₆) ppm (δ): 0.94(s, 2 \times

3H, CH₃), 1.20 (d ,1 \times 3H , CH₃) , 1.53(d ,1 \times 2H ,CH₂) , 1.87(s ,1 \times 2H ,CH₂) , 2.78(m,1 \times 1H ,CH) , 5.08(d,1 \times 1H , NCHC) , 5.44(d ,1 \times 1H ,CH- Cl) , 9.07(s ,1 \times 1H ,OH-Ar) , 6.71-7.05(s ,4 \times 1H ,CH- Ar) ,

Agilent Resolutions Pro

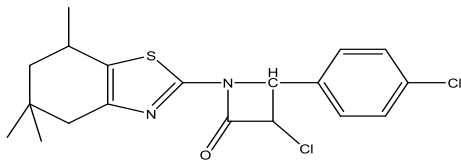


FTIR data of 3-chloro-4-(4-hydroxyphenyl)-1-(5,5,7-trimethyl-4,5,6,7-tetrahydrobenzo [d]thiazol-2-yl)azetidin-2-one



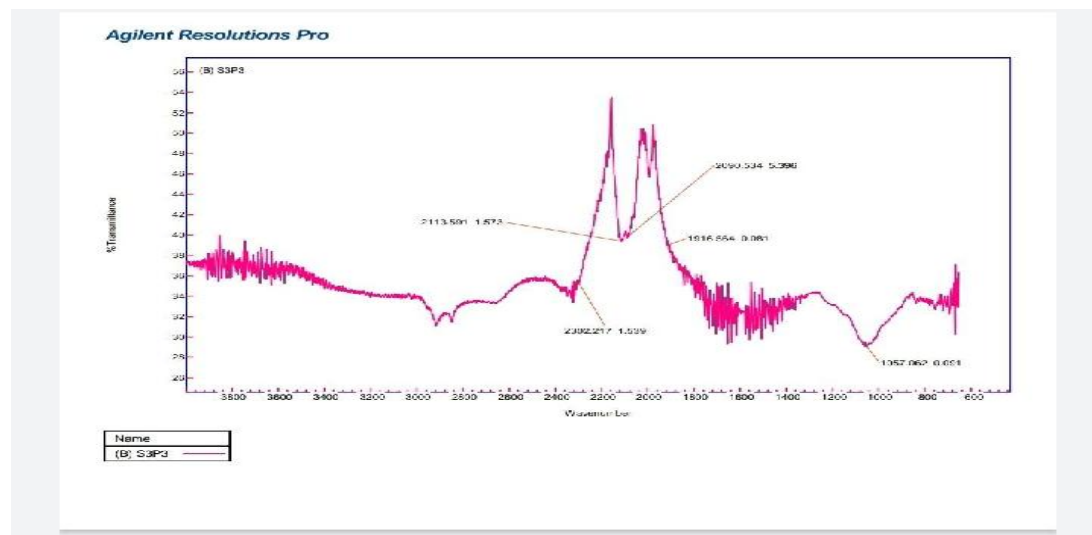
NMR data of 3-chloro-4-(4-hydroxyphenyl)-1-(5,5,7-trimethyl-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)azetidin-2-one

3c: 3-chloro-4-(4-chlorophenyl)-1-(5,5,7-trimethyl-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)azetidin-2-one

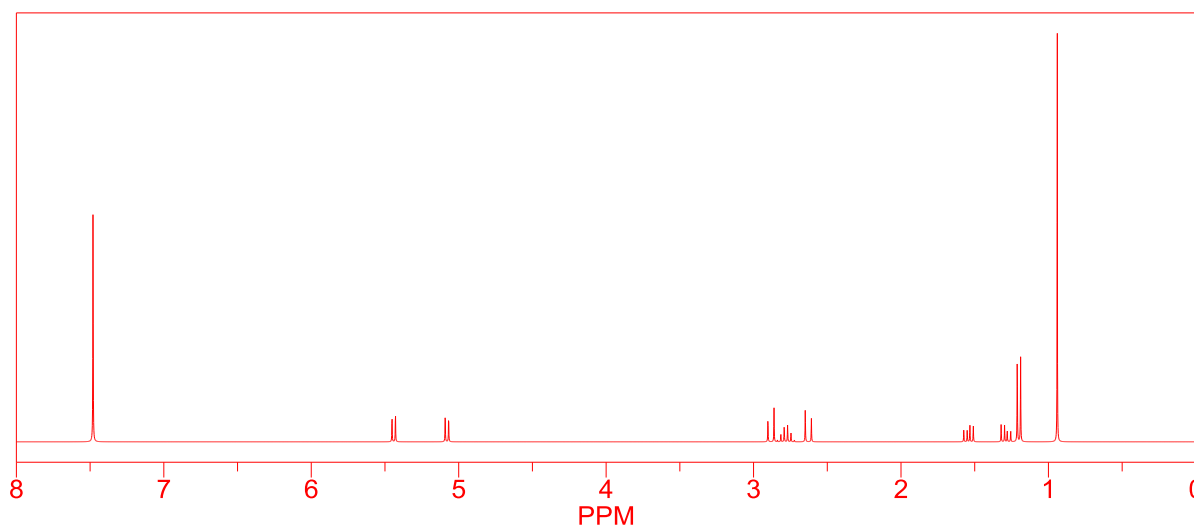


IR (KBr ν_{\max} cm^{-1}) : 752 (CH-Cl), 786 (-S-C), 1301 (-C-N), 1510 (-C-C- Ar. ring), 1565 (-C = N), 3042 (C-H ring), 1740 (C=O) 732 (CH -Cl) aromatic, ^1H NMR (CDCl₃, DMSO-d₆) ppm (δ): 0.93(s, 2 \times 3H, CH₃), 1.21(d, 1 \times 3H, CH₃), 1.54(d

, 1 \times 2H, CH₂), 2.87(s, 1 \times 2H, CH₂), 2.77(m, 1 \times 1H, C-H), 5.09(d, 1 \times 1H, NCHC), 5.44(s, 1 \times 1H, CH-Cl), 7.48(s, 4 \times 1H, CH-ring Ar),

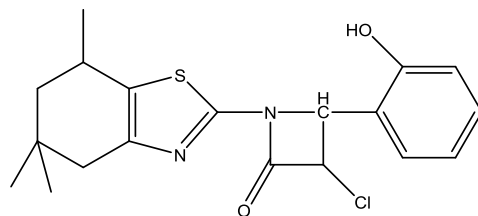


FTIR data of 3-chloro-4-(4-chlorophenyl)-1-(5,5,7-trimethyl-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)azetidin-2-one:



NMR Data of 3-chloro-4-(4-chlorophenyl)-1-(5,5,7-trimethyl-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)azetidin-2-one

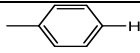
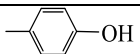
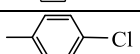


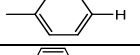
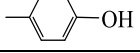
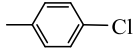
3d: 3-chloro-4-(2-hydroxyphenyl)-1-(5,5,7-trimethyl-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)azetidin-2-one :



IR (KBr ν_{\max} cm^{-1}) : 750 (CH-Cl), 786 (-S-C), 1301 (C-N), 1510 (-C-C-Ar), 1565 (-C = N), 3042 (C-H ring), 1740 (C=O) 3435 (-OH) aromatic, $^1\text{H NMR}$ (CDCl_3 , DMSO-d_6) ppm (δ): 0.94(s, 2 \times 3H, CH_3), 1.20 (d

, 1 \times 3H, CH_3), 1.54(d, 1 \times 2H, CH_2), 2.88(s, 1 \times 2H, CH_2), 2.77(m, 1 \times 1H, CH), 5.09(d, 1 \times 1H, NCHC), 5.45(d, 1 \times 1H, CH-Cl), 9.67(s, 1 \times 1H, OH-Ar), 6.83-7.12(s, 4 \times 1H, CH-Ar),

Table 1: Physical and Elemental data

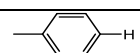
Compound No	R Group And Position	Molecular Formula	MP In $^{\circ}\text{C}$	Yield	Recrystallised Solvent	Elemental Analysis Calculated		
						C %	H %	N %
2a		$\text{C}_{17}\text{H}_{20}\text{N}_2\text{S}$	65	78	Ethanol	71.28	7.74	9.78
2b		$\text{C}_{17}\text{H}_{20}\text{N}_2\text{OS}$	68	75	Methanol	67.51	7.33	9.26
2c		$\text{C}_{17}\text{H}_{19}\text{ClN}_2\text{S}$	67	73	Ethanol	63.63	6.60	8.73
2d		$\text{C}_{17}\text{H}_{20}\text{N}_2\text{OS}$	72	68	Ethanol	67.51	7.33	9.26
3a		$\text{C}_{19}\text{H}_{21}\text{ClN}_2\text{OS}$	80	66	Methanol	62.88	6.39	7.72
3b		$\text{C}_{19}\text{H}_{21}\text{ClN}_2\text{O}_2\text{S}$	85	63	Ethanol	60.23	6.12	7.39
3c		$\text{C}_{19}\text{H}_{20}\text{Cl}_2\text{N}_2\text{OS}$	79	57	Ethanol	57.43	5.58	7.05
3d		$\text{C}_{19}\text{H}_{21}\text{ClN}_2\text{O}_2\text{S}$	82	51	Methanol	60.23	6.12	7.39

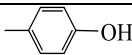
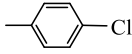
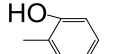
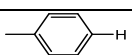
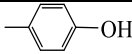
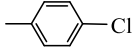
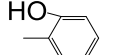
FUNGAL ACTIVITY:

New different potent derivative were synthesized and tested against their fungal properties. Antifungal properties determine and confirm by using disc diffusion procedure¹¹ against *Candida albicans*, *albicans* ATCC and *candida krusei*.

Inhibition nature of stains was checked and recorded (in mm) of different samples. Antifungal property of new synthesized compounds was compared with the standard drug fluconazole.

Table 2: Antifungal activity of compounds 2(a-d) & 3(a-d)

S.No of Compound	Compounds Formula	R Group	Fungal Inhibition Zone/mm		
			C. Albican	C. Albicans ATCC	C. Krusei
2a	$\text{C}_{17}\text{H}_{20}\text{N}_2\text{S}$		11	09	-

2b	C ₁₇ H ₂₀ N ₂ OS		16	12	7
2c	C ₁₇ H ₁₉ ClN ₂ S		21	13	9
2d	C ₁₇ H ₂₀ N ₂ OS		19	16	12
3a	C ₁₉ H ₂₁ ClN ₂ OS		23	13	11
3b	C ₁₉ H ₂₁ ClN ₂ O ₂ S		26	18	15
3c	C ₁₉ H ₂₀ Cl ₂ N ₂ OS		30	24	20
3d	C ₁₉ H ₂₁ ClN ₂ O ₂ S		28	22	16
Reference	Fluconazole	-	29	25	19

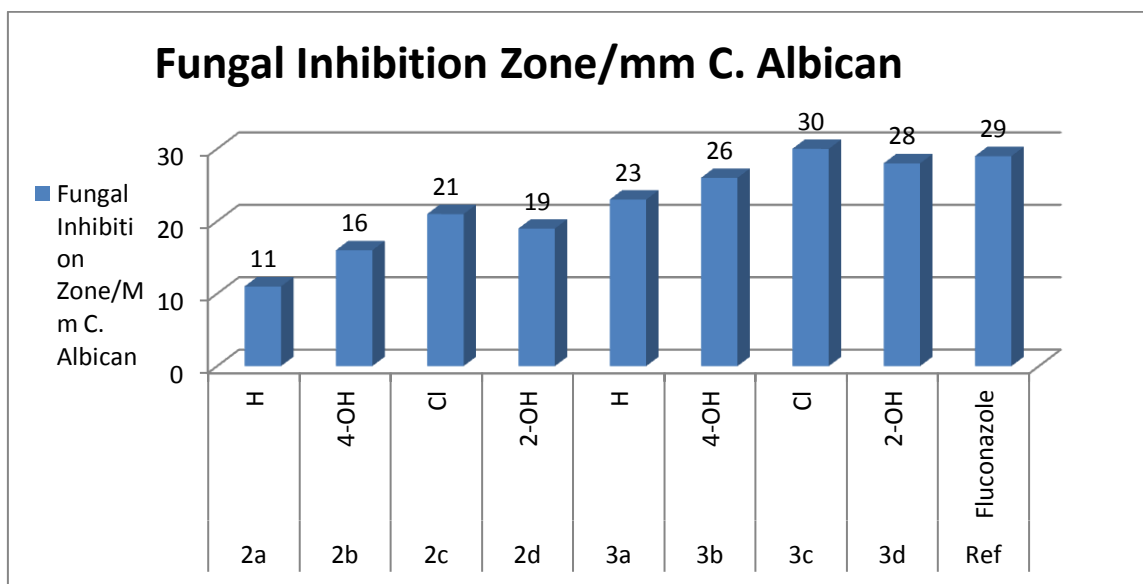


Figure 1: Inhibition Zone stain against C Albican

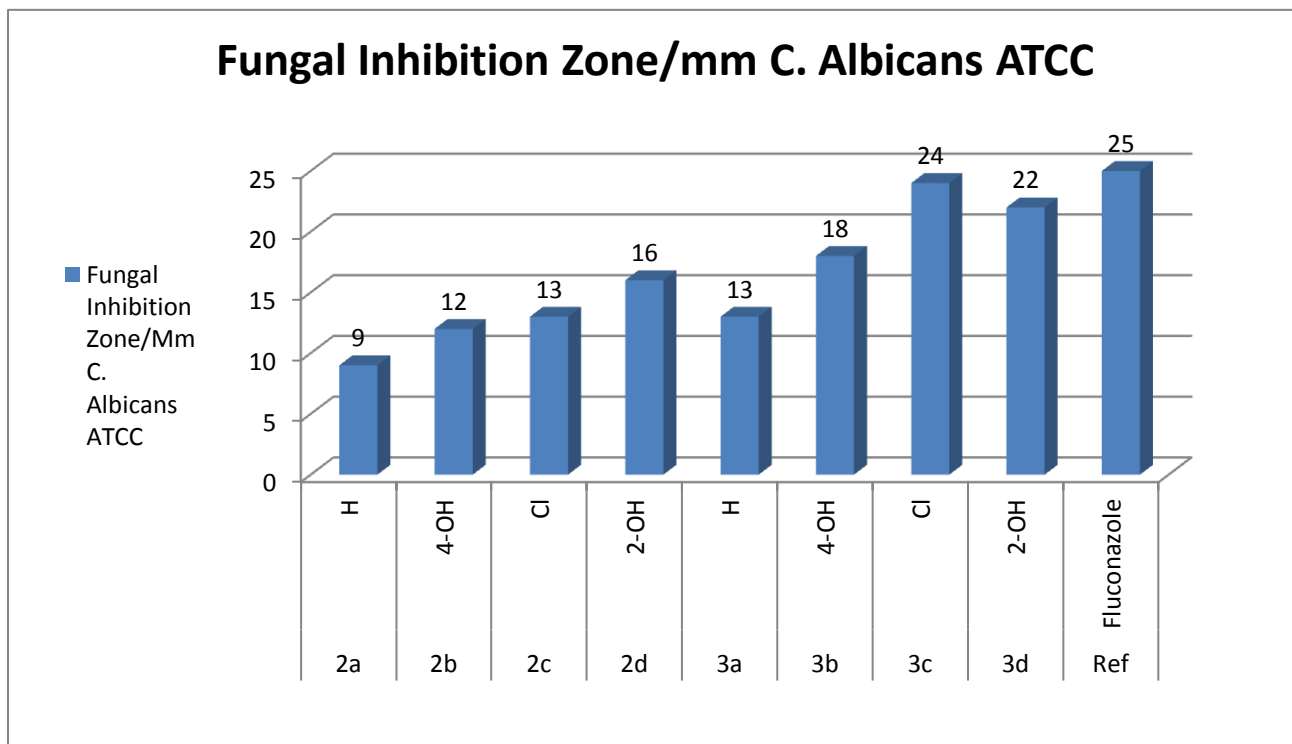


Figure 2: Inhibition Zone against C Albicans ATCC Stain

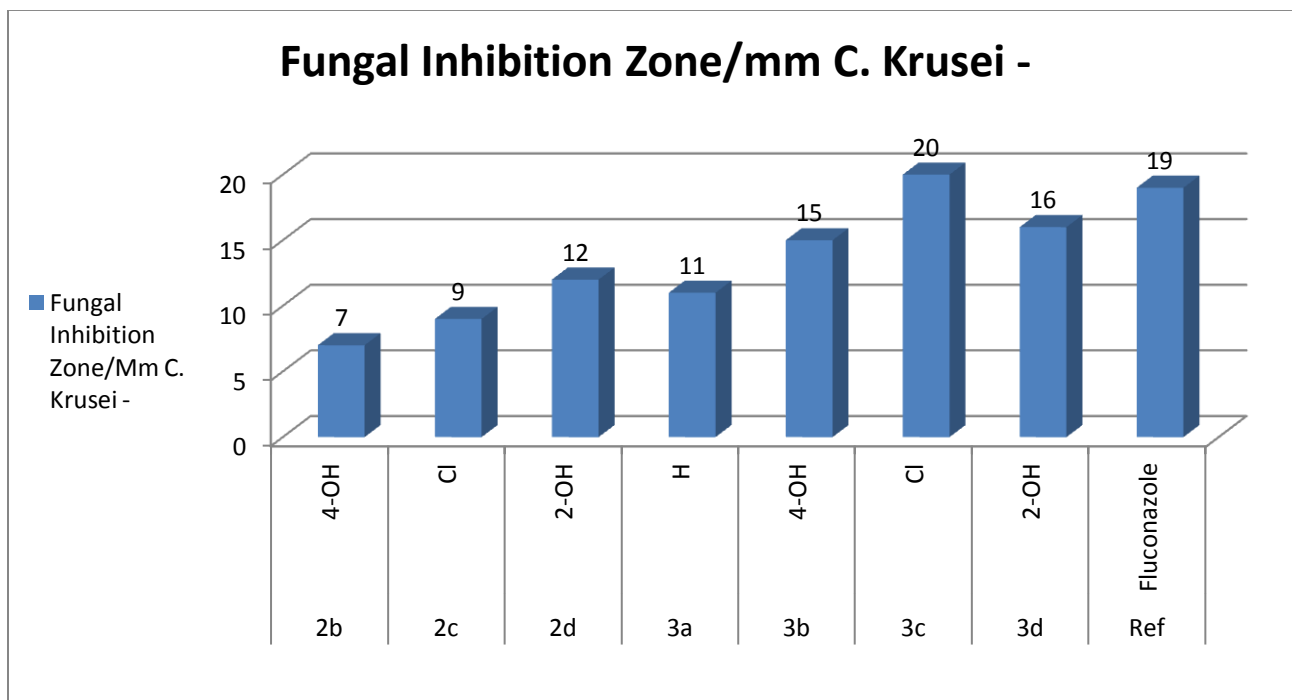


Figure 3: Inhibition Zone against C Krusei Stain

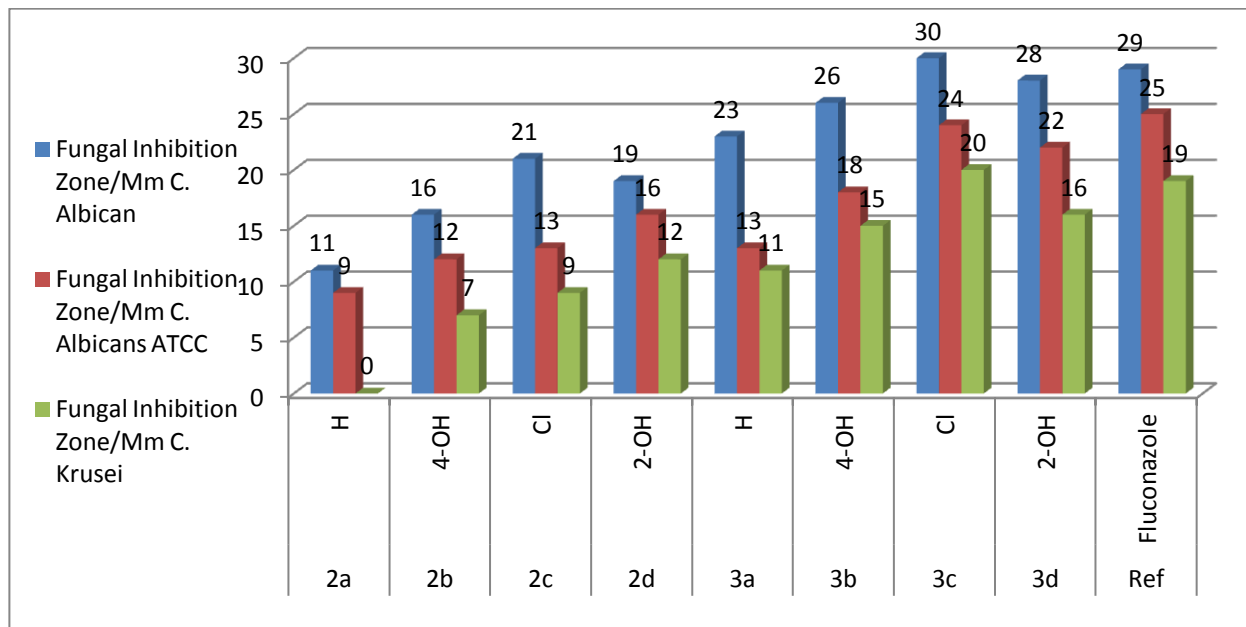


Figure 4: Comparison study Graph Represent Inhibition Effect against Different Fungi

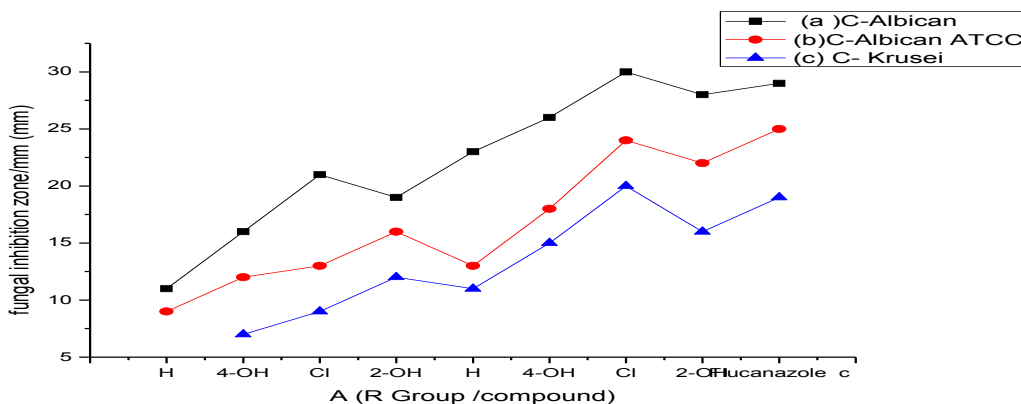


Figure 5: Comparison, study Graph Represent Inhibition Effect against Different Fungi over various ranges

RESULT AND DISCUSSION:

The new synthesized derivatives were possessed active thiazole and azetidinone nucleus. These compounds were formed in ordinary condition. Elemental analysis, molecular formula and melting point of synthesized compounds are giving in table 1. Derivatives 2(a-d) and 3(a-d) were tested against their fungal property. Its effected biological data and their values were recorded in table 2. In this experimental part, the derivatives having azetidinone with benzothiazoles moiety were exhibited better antifungal activity. In this regard Compound 3c which is the thiazol and azetidinone derivatives was found more potent antifungal against *C. albicans*, *C. albicans* ATCC, *C. krusei* and compared with standard drug fluconazole. Rest compounds were showed moderate activity against all the stains.

Spectral data of all compounds are the sequence prepared and their spectral data are recorded and evaluated and analysis these data

CONCLUSION:

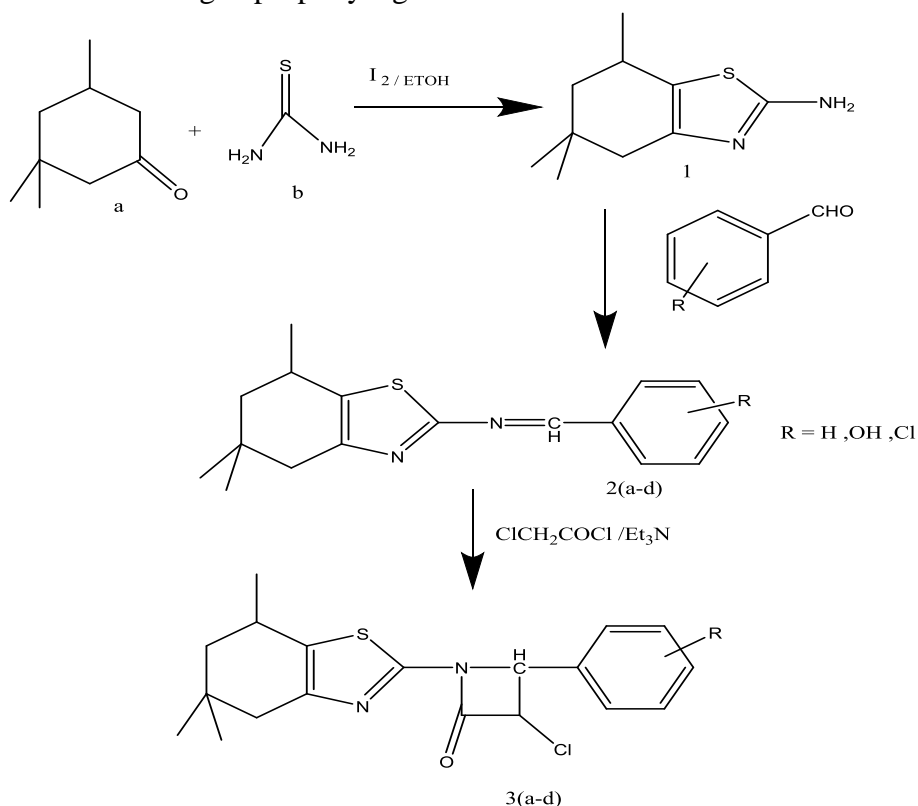
Newly novel synthesised drug derivatives of azetidinone were given the better results to protect from different class of diseases and these drugs were very useful to alive system as compare to earlier synthesis drug. These drugs were represented active antifungal in biological system. Azetidinone linkage enhances their activity of potent drugs and decreases the toxicity of novel drugs. 4-

For the compound of Schiff base 2a are recorded as IR: (KBr , v_{max} , cm^{-1}): 786 (C-S-C), 1301 (C-N), 1510 (C-C, Ar ring), 1565 (C=N), 3042 (C-H ring), 1H NMR : (DMSO- d_6 + $CDCl_3$) values of δ in ppm: 0.94 (s, 2 \times 3H, CH_3), 1.20 (d, 1 \times 3H, CH_3), 1.54 (d, 1 \times 2H, CH_2), 2.88 (s, 1 \times 2H, CH_2), 2.78 (m, 1 \times 1H, CH), 8.71 (s, 1 \times 1H, CH-N), 7.55-7.71 (s, 5 \times 1H, CH-Ar), And other compound 2b-2d similar data like 2a with some variation which support the confirmation all the synthesis molecules. Spectral data of desire compounds 3a-3d will be recorded these data of 3a, IR (KBr v_{max} cm^{-1}): 750 (CH-Cl), 786 (-S-C), 1301 (C-N), 1510 (-C-C- Ar ring), 1565 (-C=N), 3042 (C-H ring), 1735 (C=O), 1H NMR ($CDCl_3$, DMSO- d_6) ppm (δ): 0.94 (s, 2 \times 3H, CH_3), 1.20 (d, 1 \times 3H, CH_3), 1.54 (d, 1 \times 2H, CH_2), 2.88 (s, 1 \times 2H, CH_2), 5.08 (d, 1 \times 1H, NCH), 5.44 (d, 1 \times 1H, N-CH Cl), 7.27-7.36 (s, 5 \times 1H, CH-Ar) other compound 3b-3d similar data like 3a with some variation which support the confirmation all the synthesis molecules

Chloro substituted azetidinone derivatives 3c which has shown major as well as better antifungal activity i.e. 30 mm, 24mm, 20 mm against *C. albican*, *C. albican* ATCC and *C. krusei* respectively and compared with reference, standard drug fluconazole which represent the value 29 mm, 25mm, 19mm. Other compounds 3b,3d which were related derivatives of azetidenone,

aromatics substituted- OH , at 2 and 4 position , which represent the moderate value i.e. at 4-OH position 26 mm,18mm,15mm while at 2-OH position 28mm, 22mm, 16mm respectively against different fungi, Figures -1,2,3,4 were represented the proper values of inhibition zone. Figure 1st was represented the antifungal activity against C. Albicans while figure 2 was showed the affectivity against C. Albicans ATCC while figure 3 represented the antifungal properly against

C. krusei, figure 4 was indicated comparative study and information of its affectivity as antifungal towards observed stains. Figure 5 was represented the overall comparative study of inhibition nature with respective to all three represented fungi and it showed the activity in the order C albican > C albican ATCC > C krusei. A new class of 3(a-d) series of synthesis drug was very useful and it was showed clinically efficacy and low toxicity.



A propose plan to synthesis of Azetidinone Derivatives

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Conflict of interest: There is no conflict of interest.

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