Synthesis, Characterization and Biological Evaluation of Newer Chalcones by Microwave irradiation

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Abstract:

Chalcones are a common natural pigment & one of the most important classes of flavonoids & iso-flavonoids across the whole edible plant kingdom. This α, β- unsaturated carbonyl is an important and versatile intermediate for the preparation of various heterocycles. Their utility lies in their usefulness as synthons. Many research articles on chalcones were found in the literature. In this article, a series of pyridazine Chalcone derivatives were synthesized by Claisen-Schmidt condensation of 6-(3-Acetyl phenylamino) pyridazin-3(2H)-one with substituted benzaldehyde with potassium hydroxide in microwave assessed irradiation. All the synthesized derivatives(3a-o) were screened for their anti-bacterial and anti-fungal activities. Several compounds throughout the series showed moderate to good anti-bacterial and anti-fungal activity against human pathogens.

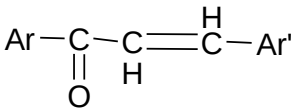
Keyword: Acetophenone, Antibacterial, Antifungal, Chalcones, Microwave, Pyridazine.

Introduction

The chemistry of chalcones is still a blossoming field. An eminent feature of the chalcones is that they

serve as the starting material for the synthesis of different classes of heterocyclic compounds. This α, β-unsaturated ketones are important and versatile intermediates for the preparation of various heterocycles.

1,3-Diaryl-2-propen-1-ones are commonly known as chalcones. They are represented as –



Their utility lies in their usefulness as synthons. Hundreds of chalcones have been isolated from natural sources and many more have been synthesized and studied over the past 50–60 years. They have received much importance in recent years because of their diverse biological activity and synthetic utility.

Chalcones are widespread components in all parts of plants and are important as flower pigments, growth regulators, Chalcones belonging to the flavonoid family [1]., which have been reported to possess a wide spectrum of biological activities, was including anti-bacterial, anti-fungal, anti-inflammatory, anti-tumour, insect anti-feed ant and anti-mutagenic [2]. Chalcones are also key precursors in the synthesis of many biologically important heterocycles such as benzothiazepine [3], Salman A. Khan (2013, p.4) have been synthesized Chalcone derivatives by the reaction of 3-acetyl-2,5-dimethylthio-phene with a corresponding active aldehyde in ethanolic NaOH in the microwave oven [4]. The structure of these compounds was established by elemental analysis.

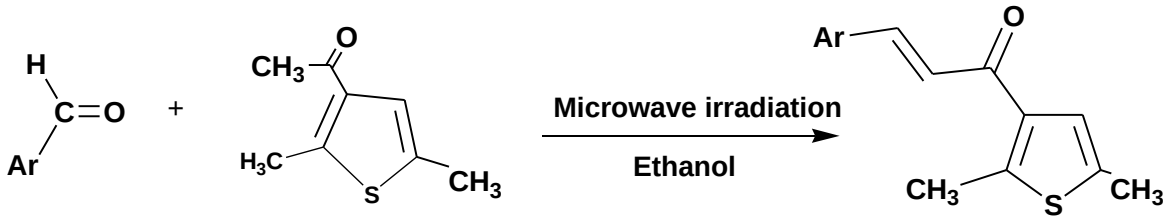


Fig. 1 Synthesis route of Chalcones

The antibacterial activity of these compounds was first tested in vitro by the disc diffusion assay against two Gram-positive and two Gram-negative bacteria, and then the minimum inhibitory concentration (MIC) was determined with the reference of standard drug Chloramphenicol. The results showed that compounds were found a better inhibitor of both types of bacteria.

Further studies using derivatives with various substitutions, and standard assay conditions are likely to be very rewarding. Chalcones constitute an important group of natural products and have been reported to possess varied biological and pharmacological activities [5]. Jadhav (2017, p.233) has been synthesized chalcone derivative by green approach using concentrated solar radiation. To check the efficacy of the process, chalcone has been synthesized by photochemical (UV radiation), thermal method (60°C) and conventional method. The effect of catalyst, concentration, and temperature on the yield of the product has been studied [6]

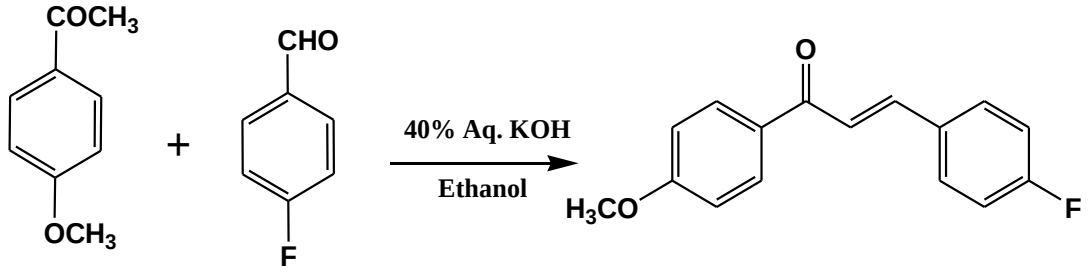
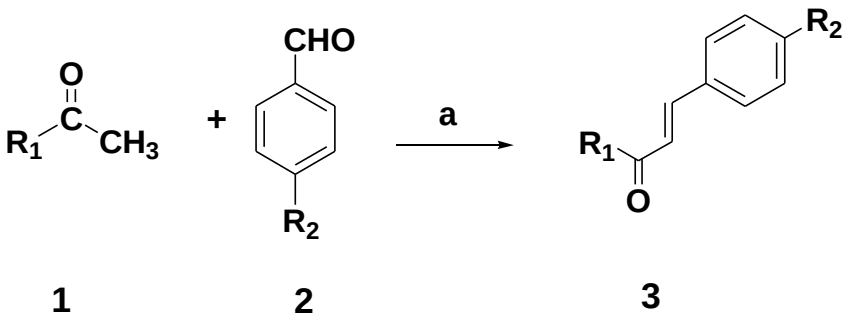


Fig. 2 Synthesis of Chalcones by green method

Marina Ritter (2015, p. 1203) were developed a green method for the synthesis of chalcones using glycerine as a solvent. Subsequently, the potential microbiology activity of these molecules was evaluated by testing them against the anti-bacterial and anti-fungal pathogens. The results showed that chalcones exhibited moderate inhibitory activity. [7]



R^1= phenyl, Thiophene

R^2 = H; -OCH_3; 4-Br; 4-Cl; 4-CH_3; 3-OCH_3

a= NaOH, Glycerine at 20°C

Fig. 3 Synthesis of Chalcones by Glycerine solvent.

Zangade (2011, p.3) developed an efficient and operationally simple reaction is shown between substituted 2-acetyl-1-naphthol/2-acetyl-1-naphthol, and different substituted benzaldehydes in presence of base afford chalcones in quantitative yield using grindstone technique.[8] Mild reaction condition, no need for catalyst, non -hazardous and environmentally safer, giving excellent yield in short reaction time, are notable advantages of this method.

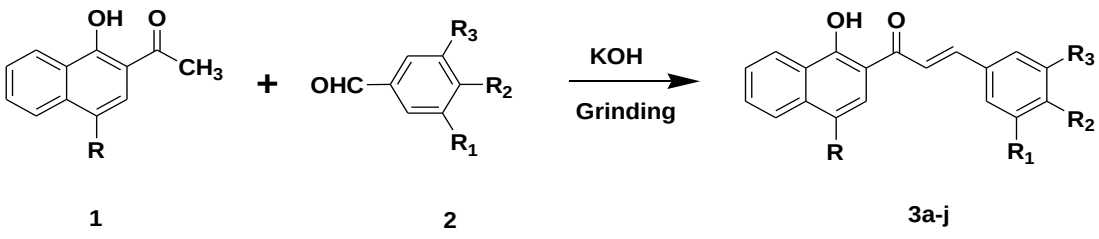


Fig. 4 Synthesis of Chalcones by Grindstone technique.

Shinde (2019, p.1) synthesized chalcone by Claisen-Schmidt condensation reaction. A series of triazine Chalcone derivatives were synthesized by the condensation of 1-(4-(4,6-dimethoxy-1,3,5-triazin-2-yl) amino) phenyl) ethenone with substituted benzaldehyde in methanol solvent. [9]

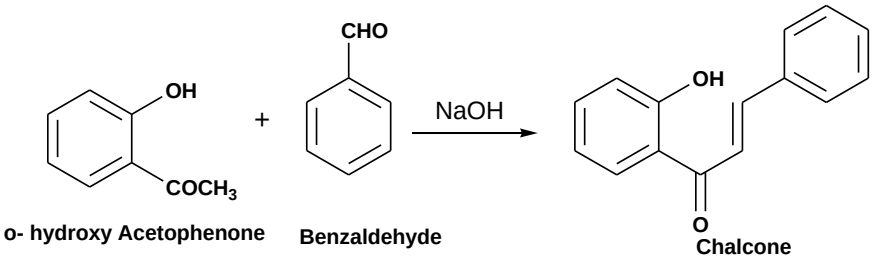


Fig. 5. Synthesis of Chalcone by Shinde (2019, p.1).

Padarthi (2013, p. 2630) have synthesized chalcones from 2-Acetyl 5-Methyl furan with various aromatic and heteroaromatic aldehydes using the method of Aldol condensation.[10]

Ahmada (2016, p. 933) Synthesized novel chalcone derivatives by conventional and microwave irradiation method and their pharmacological activities. By microwave-assisted synthesis, a considerable increase in the reaction rate has been observed and that too, with better yields [11].

Tupare (2012, p. 527) Synthesized chalcone derivatives by microwave irradiation method by using mixture of aldehydes, acetophenone and Eaton's reagent. under microwave irradiation [12]. Eaton's reagent is suitable for synthesis of chalcones of different functional groups Catalytic amount of Eaton's is sufficient for maximum conversion with high yields in short reaction time.

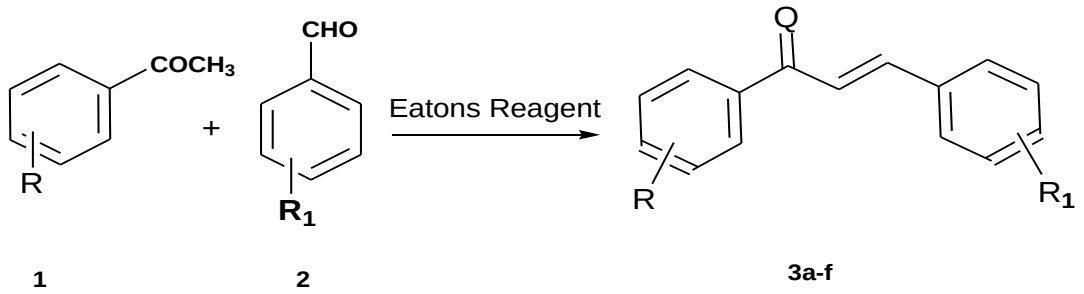


Fig. 5. Synthesis of Chalcone by Tupare (2012, p.577).

By microwave-assisted synthesis, a considerable increase in the reaction rate has been observed and that too, with better yields.

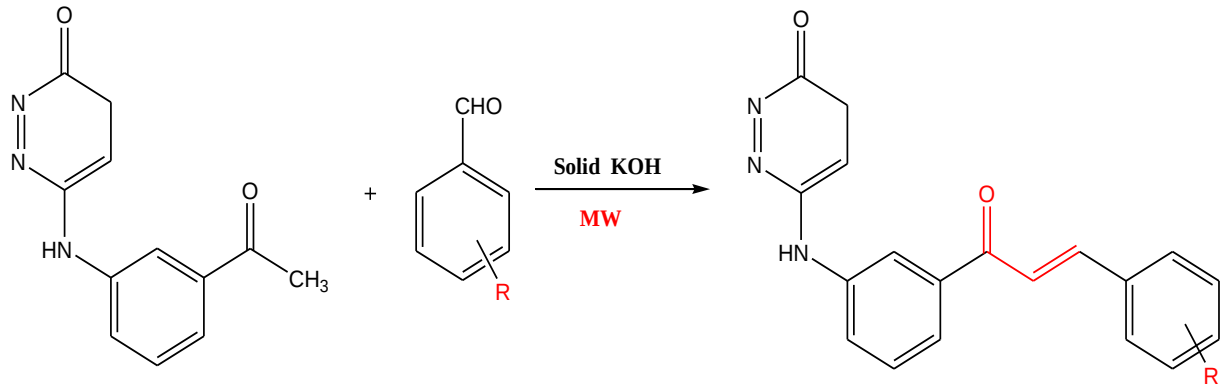
The utility of Chalcones due to their usefulness as in synthesis of various heterocyclic compounds, as plant origin and exhibit anti-malarial [13], anti-bacterial [14], anti-fibrogenic [15], anti-cancer [16], anti-chromonal [17], anti-inflammatory [18], anti-leishmanial [19], cytotoxic, and anti-trypanosome Cruzi [20] activities.

Many derivatives of chalcones were prepared from hydroxyl acetophenones containing aryl and naphthyl rings by Claisen-Schmidt condensation reaction. In this study, we synthesized Pyridazine Chalcone and evaluated them for their anti-bacterial and anti-fungal activities. Here, newly prepared 6-(3-acetylphenylamino) pyridazin-3(2H)-one treated with a substituted aldehyde in alkaline medium & irradiated in a domestic microwave oven using solid KOH. Microwave-induced organic reaction enhancement chemistry is gaining popularity as a non-conventional technique for rapid organic synthesis. This technique is easy access to very high temperature, good control over energy input in a reaction, higher yields and rapid synthesis of organic compounds. All these chalcones have been assessed for their microbial activity**.**

2. THEORETICAL

Here we have reported the synthesis of Pyridazine Chalcones(3a-o). The chemicals used were of Laboratory Reagent grade. The 6-(3-acetyl phenylamino) pyridazin-3(2H)-one was used for the synthesis of respective newer chalcones. The purity of synthesized chalcones was checked by TLC on alumina `Silica gel plates. The spots were exposed in the iodine chamber. The structures of the chalcones were assigned on the basis of spectral data (IR, 1H NMR, and Mass). All resultant chalcones compounds were screened for their antibacterial and antifungal activity.

Scheme 1: Synthesis of newer pyridazine chalcones (3a-o)



1 **2** **Chalcones (3a-o)**

Fig. 6. Synthesis of Chalcones by Pyridazine ring derivatives

R=3a-o

Sr. No.	**R**	**Sr No**	**R**
3a	-H	3i	4-OCH_3
3b	3,4-OCH_3	3j	2-NO_2
3c	4-OH	3k	3,4,5- OCH_3
3d	2-OH	3l	2,6-Cl
3e	2-Br, 4-OCH_3	3m	4-F
3f	3-NO_2	3n	3,4-OH
3g	4-Cl	3o	3,5- OCH_3
3h	4-NO_2		

3. EXPERIMENTAL WORK

All the Chemical used in this synthesis are AR grades. Melting points were measured with the open glass capillary method and were uncorrected.

The purities of the compounds were checked on silica-gel-coated Al plates. IR spectra were recorded in KBr on a Perkin Elmer Spectrum BX series FT-IR spectrometer. ^{1}H- NMR spectra are recorded in DMSO-d6 on Bruker DRX 300 MHz NMR spectrometer. The chemical shift is expressed in δ unit with TMS as internal standard and mass spectra were obtained on a Joel D-300 spectrometer in SAIF, Indian Institute of Bombay, Mumbai, India

3.1. General Method for the Synthesis of Pyridazine Chalcones (3a-o)

Equimolar quantities of acetophenone (6-(3-Acetyl phenyl amino) pyridazin-3(2H)-one**)** and different aromatic aldehyde & catalytic quantity of solid KOH (0.05g) mixed over an ice bath. The reaction flask was loosely corked and kept at 180 W in a domestic oven [21] for about 3.5 - 4 minutes with an interval of 30 seconds. The contents of the flask were then diluted with H_2O and acidified with HCl (10%). The solid obtained was filtered, washed with cold water, dried and, recrystallized from a suitable solvent. The M.P., yields, and percentage of yield are shown in Table 1.

The purity of synthesized chalcones was checked by TLC on microscopic slide with `Silica gel-G' layers. The spots were exposed in iodine chamber. The structures of the chalcones were assigned on the basis of spectral data (IR, ^{1}H NMR and Mass).

3.2. Preparation of 6- (3- ((E) -4- (3,4-dimethoxyphenyl) but- 3- enoyl) phenylamino) pyridazin -3 (2H) one (3g)

The 6-(3-acetylphenylamino) pyridazin-3(2H)-one (0.02 mole) and 4-chloro benzaldehyde (0.02 mole) were well mixed with one pallet of solid KOH over an ice bath. Then the reaction flask was loosely corked and kept 180 W in a domestic oven for 4.0 minutes with an interval of 30 seconds. After 4 minutes the reaction mixture was diluted with H_2O and acidified with HCl (10%). The separated solid was filtered and crystallised from glacial acetic acid to give **3g**.

Similarly, other compounds of series were also prepared by same procedure. The melting points, yields, elemental analyses of different chalcones are listed in Table 1.

4. RESULT AND DISCUSSIONS

A variety of methods were reported in the literature for the preparation of chalcones. But the most acceptable method is Claisen Schmidt Condensation. The conventional method of synthesis required 18-22 hrs to obtain the product of chalcones, therefore researchers discovered alternative methods of synthesis of chalcones in which by using a catalyst, microwave, Ultrasound waves, etc. Here, we have synthesized chalcones by microwave irradiation method. The yield of substituted derivatives of chalcones was synthesized by the green chemistry principle i.e. time and energy - saving were found to be in the range of 65- 85%. The purity of compounds was ascertained by the melting point and TLC. The structure of newer synthesized compounds was assigned on the basis of IR spectroscopy,

^{1}HNMR, Mass spectroscopy and elemental analysis. Compound (3a-o) shows the characteristics absorption band at 1682, 1675 cm^{-1}due to carbonyl (-C=O) group & 1515 cm^{-1} due to (-CH=CH-, Str.); The ^{1}HNMR of compounds (3a-O) showed doublet at δ 6.95 -7.0 Hz due to -COCH=CH; and doublet at δ 7.42-7.44 Hz due to Ar-CH=CH which indicates the presence of Chalcone Moiety. All synthesized chalcones were screened for their antibacterial and antifungal activities. Compound numbers (Table No. II), **3a, 3c, 3h, 3n** and **3o** shows antibacterial activities against ***E. Coli.*** pathogens, whereas **3a, 3c, 3g, 3k, 3l, 3n** were active against ***S. aureus***. In case of antifungal activities compound nos. **3g, 3h,** and **3m** found active against **Aspergillus *Niger*.** Whereas **3a, 3f, 3g, 3i, 3j, 3l and 3n** found active against Candida ***Albicans***. From above observation it's clear that novel synthesized chalcones were microbial active.

5. ANTIMICROBAIAL ACTIVITY

An antimicrobial is a substance that kills or inhibits the growth of bacteria, fungi, or viruses. Bacteria are involved in many aspects of ecology and health. These bacteria are used for making yogurt, curd, cheese, and other fermented foods. A large number of bacteria living on the skin and in the digestive tract. Escherichia coli is a gram-negative bacterium that is commonly found in the lower portion of the intestine and urinary tract of warm-blooded organisms. Staphylococcus aureus is the gram-positive non-motile cocci arranged in groups. All of the substituted chalcones were screened for their antibacterial and antifungal activity against the Gram -ve bacteria Escherichia coli (ATCC8739) and Gram +ve bacteria Staphylococcus aureus (ATCC6538), in addition to their antibacterial activity against Aspergillus Niger (ATCC16404), Candida Albicans (ATCC10231) using agar diffusion

method. [22,23] at a concentration 20mg/mL. DMSO used as a solvent. Standard Penicillin and Griseofulvin were used as antibacterial and antifungal. Some of the compounds found more active than standard. 3a, 3c, 3h, 3n, and 3o shows antibacterial activities against E. Coli. pathogens, whereas 3a, 3c, 3g, 3k, 3l, 3n were active against S. aureus. In the case of antifungal activities compound nos. 3g, 3h, and 3m found active against Aspergillus Niger. Whereas 3a, 3f, 3g, 3i, 3j, 3l, and 3n found active against Candida Albicans.

The results, recorded as average diameter of inhibition zone in mm, are given in table 2.

6. SUPPLEMENTARY DATA OF PYRIDAZINE CHALCONES

6.1. Characterization data for synthesised compounds (3a-o) are given below:

6.1.1. Characterization data for compound 6-(3-((E)-3-phenyl acryloyl) phenyl amino) pyridazin-3(2H)-one (3a): Nature: Pale Yellow solid; M. F. $C_{19}H_{15}N_3O_2$; Yield **67**% , M. P. 192 ^{0}C; **IR (KBr)**: 3244(Ar.C=C Str.), 3300 (N-H Str.), 1665, 1670 (C=O),1522 (-CH=CH-, Str.); **^{1}H NMR (DMSO-d_6)**: δ 7. 28 (d, 1H, Jα,β =16Hz, H β), 6.92-7.15 (m, 5H, Ar-H), 6.94-7.15 (m, 5H, Ar-H), 6.80-6.88 (d, 1H J=9.8 Hz, CH pyridazine), 7.18-7.23 (d, 1H, J= 9.9 Hz, CH Pyridazine), 6.99 (d, 1H, -CO-CH=) 7.35-7.45 (d, 1H, J= 7.8Hz, Ar-CH=), 7.48-7.52 (t, 1H, NH pyridazine D_2O exchangeable); **Mass** (m/z): 317, [M^+, 100%]; **Elemental Analysis** (% for) $C_{19}H_{15}N_3O_2$ Calcd. C, 72.00; H, 4.75; N, 13.39; O, 9.95; found. C, 71.70; H, 4.40; N, 12.40; O, 9.80.

6.1.2. Characterization data for compound 6-(3-((E)-3-(3, 4-dimethoxyphenyl)acryloyl)phenylamino)pyridazin-3(2H)-one(3b): Natur: Dark Yellow solid; M. F. $C_{21}H_{19}N_3O_4$; Yield 77% , M. P. 185^{0}C; **IR(KBr):** 3300 (Ar, C=C Stre.), 3250 (N-H Stre.), 1685, 1680 (2 C=O), 1500 (-CH=CH-, str.);

^{1}H NMR (DMSO-d_6): 3.75 (s, 6H, -OCH_3), δ 7. 28 (d, 1H, Jα,β= 16Hz, H β), 6.78-7.25 (m, 4H, Ar-H), 6.865-7.20 (m, 4H, Ar-H), 6.83-6.90 (d, 1H J=9.8 Hz, CH pyridazine), 7.17-7.22 (d, 1H, J=9.9 Hz CH Pyridazine), 7.55 (d, 1H, -CO-CH=), 7.55-7.70 (d, 1H J= 7.8Hz Ar-CH=), 4.4 (t, 1H, NH pyridazine D_2O exchangeable);

Mass;(m/z): 377, [M^+, 100%], **Elemental Analysis** (% for) $C_{21}H_{19}N_3O_4$ Calcd. C 66.86; H 5.00; N 11.13; O 17.08; found. C 67.00; H 5.10; N 11.00; O 17.11.

6.1.3. Characterization data for compound 1. 6-(3-((E)-3-(4-hydroxyl phenyl) acryloyl) phenyl amino) pyridazin-3(2H)-one (3c):

Nature: Pale Yellow solid; M. F. $C_{19}H_{15}N_3O_3$; Yield 66% , M. P. 155 ^{0}C; **IR (KBr)**: 3240 (Ar.C=C Str.), 3250 (N-H Str.), 1682, 1675 (>C=O), 3344 (-OH); 1515 (-CH=CH-, Str.); **^{1}H NMR (DMSO-d_6)**: 6.75-7.15 (m, 4H, Ar-H), 6.75-7.20 (m, 4H, Ar-H), 3.1 (d, 2H J=9.8 Hz, CH pyridazine), 5.2 (t, 1H, J= 9.9 Hz, CH Pyridazine), 7.60 (d, H, -CO-CH_2-),7.92-7.94 (d, 1H, J= 7.8Hz, Ar-CH=), 4.2 (s, 1H, NH pyridazine D_2O exchangeable); 5.2 (s, H, D_2O exchangeable **)**; **Mass** (m/z): 333, [M^+, 100%]; **Elemental Analysis** (% for) $C_{19}H_{15}N_3O_3$; Calcd. C, 68.45; H, 4.55; N, 12.69; O, 14.35; found. C, 68.55; H, 4.30; N, 12.45; O, 14.00.

6.1.4. Characterization data for compound 6-(3-((E)-3-(2-hydroxyphenyl)acryloyl)phenylamino)pyridazin-3(2H)-one (3d): Nature: Yellow solid; M. F. $C_{19}H_{15}N_3O_3$; Yield 60% , M. P. 145^{0}C; **IR(KBr):** 3265 (Ar, C=C Str.), 3220 (N-H Str.), 1685, 1677 (>C=O), 3260 (-OH); 1518 (-CH=CH-, str.); 3260 (-OH); **^{1}H NMR (DMSO-d_6)**: 6.65-7.12 (m, 4H, Ar-H), 6.75-7.20 (m, 4H, Ar-H), 3.08 (d, 2H J=9.8 Hz, CH pyridazine), 5.4 (t, 1H, J= 9.9 Hz, CH Pyridazine), 7.40 (d, H, -CO-CH-),8.12 (d, 1H, J= 7.8Hz, Ar-CH=), 3.9 (s, 1H, NH pyridazine D_2O exchangeable); 5.0 (s, H, D_2O exchangeable **)**; **Mass;(m/z)**: 333, [M^+, 100%], **Elemental Analysis** (% for) $C_{19}H_{15}N_3O_3$ Calcd. C, 68.46; H, 4.50; N, 12.63; O, 14.42; found. C 68.88; H, 4.35; N, 12.35; O, 14.15.

6.1.5. Characterization data for compound 1. 6-(3-((E)-3-(2-bromo-3, 4-dimethoxy phenyl) acryloyl) phenyl amino) pyridazin-3(2H)-one (3e):

Nature: DeepYellow solid; M. F. $C_{21}H_{18}BrN_3O_4$; Yield **82**% , M. P. 190 ^{0}C; **IR (KBr)**: 3240(Ar.C=C Stre.), 3200 (N-H Stre.), 1682, 1675 (2 C=O),1515 (-CH=CH-, Str.); **^{1}H NMR (DMSO-d_6)**: 3.75 (s, 6H, 3,4-OCH_3), 6.90-7.30 (dd, 2H, Ar-H), 6.65-7.12 (m, 4H, Ar-H), 3.09 (d, 2H J=9.8 Hz, CH pyridazine), 5.5 (t, 1H, J= 9.9 Hz, CH Pyridazine), 7.38 (d, 1H, -CO-CH-),8.20 (d, 1H, J= 7.8Hz, Ar-CH=), 4.2 (s, 1H, NH pyridazine D_2O exchangeable); **Mass** (m/z): 457,

[M^+, 100%]; **Elemental Analysis** (% for) $C_{21}H_{18}BrN_3O_4$ Calcd. C, 55.27; H, 3.95; Br, 17.50; N, 09.19; O, 14.05; found. C, 55.30; H, 3.90; Br, 17; N, 09.18; O, 14.00.

6.1.6. Characterization data for compound 6-(3-((E)-3-(3-nitrophenyl) acryloyl) phenyl amino) pyridazin-3(2H)-one (3f):

Natur: Faint Red solid; M. F. $C_{19}H_{14}N_4O_4$; Yield 80% , M. P. 190^{0}C; **IR(KBr):** 3254 (Ar, C=C Str.), 3235 (N-H Str.), 1675, 1678 (C=O), 1522 (-CH=CH-, str.); 1372 (NO_2); **^{1}H NMR (DMSO-d_6)**: 7.50-8.30 (dd, 4H, Ar-H), 6.75-7.20 (m, 4H, Ar-H), 3.1 (d, 2H J=9.8 Hz, CH pyridazine), 5.4 (t, 1H, J= 9.9 Hz, CH Pyridazine), 7.85 (d, 1H, -CO-CH-), 8.00 (d, 1H, J= 7.8Hz, Ar-CH=), 4.01 (s, 1H, NH pyridazine D_2O exchangeable); **Mass;(m/z)**: 362, [M^+, 100%], **Elemental Analysis** (% for) $C_{19}H_{14}N_4O_4$ Calcd. C 62.96; H 3.90; N 15.43; O 17.68; found. C 62.93; H 4.30; N 15.33; O 17.61.

6.1.7. Characterization data for compound 1. 6-(3-((E)-3-(4-chlorophenyl) acryloyl) phenyl amino) pyridazin-3(2H)-one (3g):

Nature: Pale Yellow solid; M. F. $C_{19}H_{14}ClN_3O_2$; Yield **77**% , M. P. 192 ^{0}C; **IR (KBr)**: 3240(Ar.C=C Stre.), 3220 (N-H Str.), 1680, 1675 (>C=O),1518 (-CH=CH-, Str.); 765(-Cl); **^{1}H NMR (DMSO-d_6)**: 7.20-7.24 (m, 4H, Ar-H), 6.74-7.22 (m, 4H, Ar-H), 3.06 (d, 2H J=9.8 Hz, CH pyridazine), 5.5 (t, 1H, J= 9.9 Hz, CH Pyridazine), 7.55 (d, 1H, -CO-CH-), 7.92 (d, 1H, J= 7.8Hz, Ar-CH=), 4.0 (s, 1H, NH pyridazine D_2O exchangeable); **Mass** (m/z): 351, [M^+, 100%]; **Elemental Analysis** (% for) $C_{19}H_{14}ClN_3O_2$ Calcd. C, 65.66; H, 4.45; Cl, 10.10; N, 11.58; O, 8.95; found. C, 65.70; H, 4.40; Cl, 10.00; N, 11.88; O, 9.00.

6.1.8. Characterization data for compound 6-(3-((E)-3-(4-nitrophenyl) acryloyl) phenylamino) pyridazin-3(2H)-one (3h):

Nature: Reddish solid; M. F. $C_{19}H_{14}N_4O_4$; Yield 80% , M. P. 182^{0}C; **IR(KBr):** 3260 (Ar, C=C Stre.), 3250 (N-H Stre.), 1685, 1670 (>C=O), 1518 (-CH=CH-, str.); 1370 (-NO_2)

^{1}H NMR (DMSO-d_6): 7.50-8.14 (m, 4H, Ar-H), 6.74-7.24 (m, 4H, Ar-H), 3.06 (d, 2H J=9.8 Hz, CH pyridazine), 5.45 (t, 1H, J= 9.9 Hz, CH Pyridazine), 7.86 (d, 1H, -CO-CH-), 8.05 (d, 1H, J= 7.8Hz, Ar-CH=), 4.0 (s, 1H, NH pyridazine D_2O exchangeable);**Mass;(m/z)**: 362, [M^+, 100%], **Elemental Analysis** (% for) $C_{19}H_{14}N_4O_4$; Calcd. C 62.96; H 3.90; N 15.43; O 17.68; found. C 62.98; H 4.30; N 15.43; O 17.61.

6.1.9. Characterization data for compound 6-(3-((E)-3-(4-methoxyphenyl) acryloyl) phenylamino) pyridazin-3(2H)-one (3i):

Natur: Yellow solid; M. F. $C_{20}H_{17}N_3O_3$; Yield 76% , M. P. 138^{0}C; **IR(KBr):** 3260 (Ar, C=C Stre.), 3250 (N-H Stre.), 1685, 1670 (2 C=O), 1518 (-CH=CH-, str.); **^{1}H NMR (DMSO-d_6)**: 3.95 (s, 3H, 4-OCH_3), δ 7. 28 (d, 1H, Jα,β= 16Hz, H β), 6.88-7.33 (m, 5H, Ar-H), 6.88-7.15 (m, 5H, Ar-H), 6.83-6.90 (d, 1H J=9.8 Hz, CH pyridazine), 7.17-7.22 (d, 1H, J=9.9 Hz CH Pyridazine), 6.95 (d, 1H, -CO-CH=), 7.42-7.44 (d, 1H J= 7.8Hz Ar-CH=), 7.51-7.54 (t, 1H, NH pyridazine D_2O exchangeable); **Mass;(m/z)**: 347, [M^+, 100%], **Elemental Analysis** (% for) $C_{20}H_{17}N_3O_3$ Calcd. C 69.16; H 4.90; N 12.25; O 14.00; found. C 69.00; H 4.10; N 14.05; O 13.90.

6.1.11. Characterization data for compound 1. 6-(3-((E)-3-(3, 4, 5-trimethoxyphenyl) acryloyl) phenyl amino) pyridazin-3(2H)-one (3k):

Nature: Dark Yellow solid; M. F. $C_{22}H_{21}N_3O_5$; Yield **75**%, M. P. 161^{0}C; **IR (KBr)**: 3240 (Ar.C=C Str.), 3200 (N-H Str.), 1682, 1675 (2 C=O),1515 (-CH=CH-, Str.); **^{1}H NMR (DMSO-d_6)**: 3.74 (s, 9H, 3,4,5-OCH_3), 6.30 (dd, 2H, Ar-H), 6.74-7.18 (m, 4H, Ar-H), 3.06 (d, 2H J=9.8 Hz, CH pyridazine), 5.4 (t, 1H, J= 9.9 Hz, CH Pyridazine), 7.58 (d, 1H, -CO-CH-),8.00 (d, 1H, J= 7.8Hz, Ar-CH=), 4.0 (s, 1H, NH pyridazine D_2O exchangeable);**Mass** (m/z): 407, [M^+, 100%]; **Elemental Analysis** (% for) $C_{22}H_{21}N_3O_5$ Calcd. C, 64.88; H, 5.25; N, 10.29; O, 19.65; found. C, 65.00; H, 5.20; N, 10.31; O, 19.70.

6.1.10. Characterization data for compound 6-(3-((E)-3-(2, 6-di

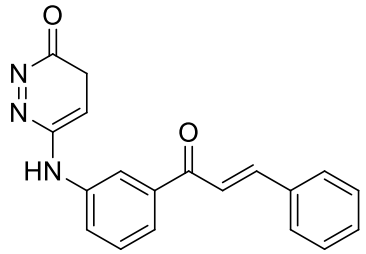
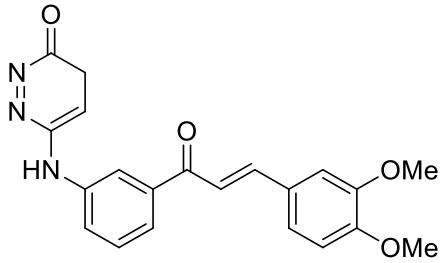
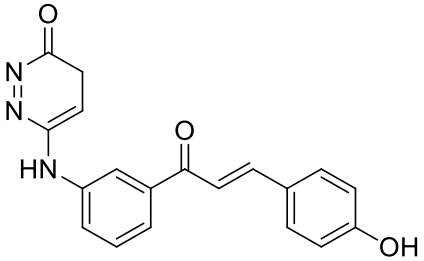
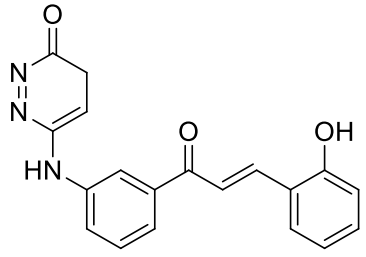
chlorophenyl)acryloyl)phenylamino)pyridazin-3(2H)-one (3l): Natur: Yellow solid; M. F. $C_{21}H_{19}N_3O_3$; Yield 61% , M. P. 193^{0}C; **IR(KBr):** 3267 (Ar, C=C Str.), 3230 (N-H Str.), 1675, 1677 (>C=O), 1522 (-CH=CH-, str.); 765(-Cl); **^{1}H NMR (DMSO-d_6)**: 7.00-7.12 (m, 3H, Ar-H), 6.78-7.22 (m, 4H, Ar-H), 3.09 (d, 2H J=9.8 Hz, CH pyridazine),

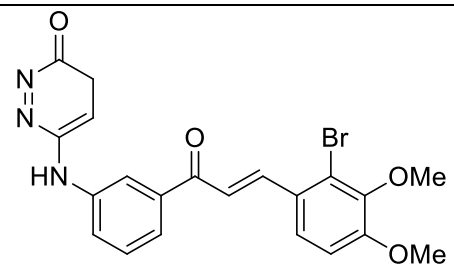
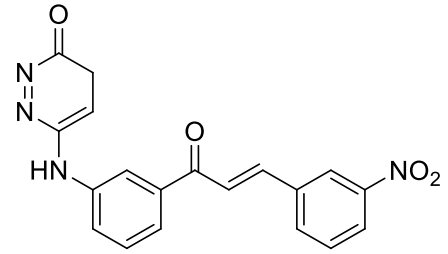
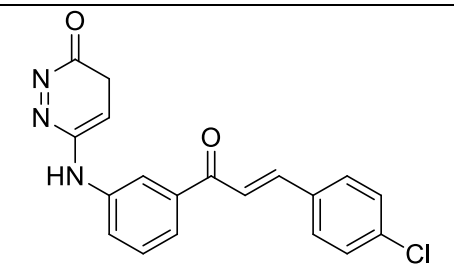
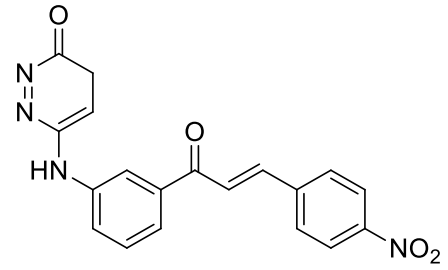
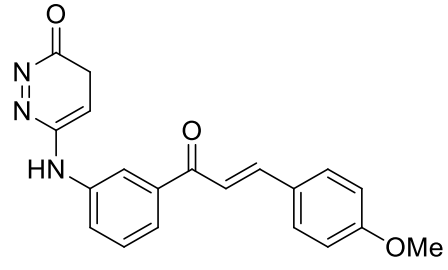
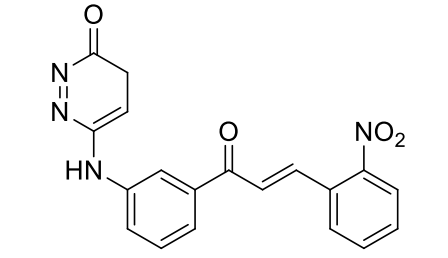
5.4 (t, 1H, J= 9.9 Hz, CH Pyridazine), 7.42 (d, 1H, -CO-CH-),8.16 (d, 1H, J= 7.8Hz, Ar-CH=), 4.05 (brs, 1H, -NH pyridazine D_2O exchangeable); **Mass;(m/z)**: 361, [M^+, 100%], **Elemental Analysis** (% for) $C_{21}H_{19}N_3O_3$ Calcd. C 69.76; H 5.30; N 11.63; O 13.28; found. C 69.88; H 5.30; N 11.33; O 13.11.

6.1.11. Characterization data for compound 6-(3-((E)-3-(3, 5-dimethoxy phenyl) acryloyl) phenyl amino) pyridazin-3(2H)-one (3o):

Nature: Pale Yellow solid; M. F. $C_{21}H_{19}N_3O_4$; Yield **85**% , M. P. 190 ^{0}C; **IR (KBr)**: 3240(Ar.C=C Stre.), 3200 (N-H Stre.), 1682, 1675 (2 C=O),1515 (-CH=CH-, Str.); **^{1}H NMR (DMSO-d_6)**: 3.74 (s, 6H, 2-OCH_3), 6.18-6.35 (m, 3H, Ar-H), 6.76-7.20 (m, 4H, Ar-H), 3.1 (d, 2H J=9.8 Hz, CH pyridazine), 5.6 (t, 1H, J= 9.9 Hz, CH Pyridazine), 7.56 (d, 1H, -CO-CH-), 7.90 (d, 1H, J= 7.8Hz, Ar-CH=), 4.0 (s, 1H, NH pyridazine D_2O exchangeable); **Mass** (m/z): 349, [M^+, 100%]; **Elemental Analysis** (% for) $C_{21}H_{19}N_3O_4$, Calcd. C, 66.88; H, 5.10; N, 11.16; O, 16.96. O, 8.98; found. C, 66.88; H, 5.10; N, 11.16; O, 16.96.

Table 1 Physical Data of Substituted Chalcones.

Entry	Structure of Compound	Yield (%)	Time in (Minutes)	M. p. (°C)
3a		65	4	192
3b		77	3.5	185
3c		66	4	155
3d		60	4.5	145

3e		82	3.5	190
3f		80	4	190
3g		77	4	192
3h		80	4.5	182
3i		76	4	138
3j		89	4.5	150

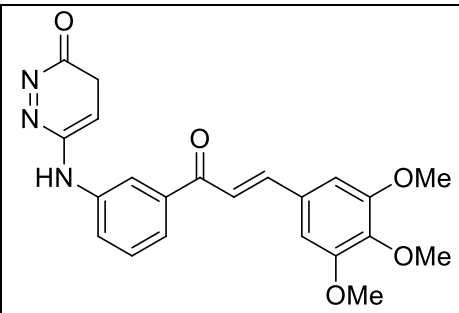
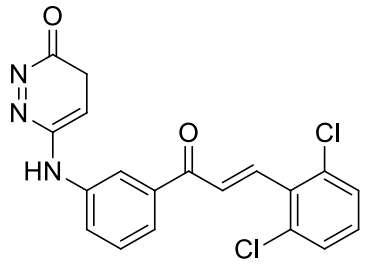
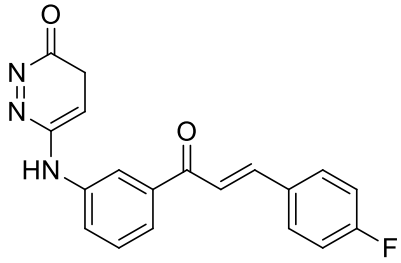
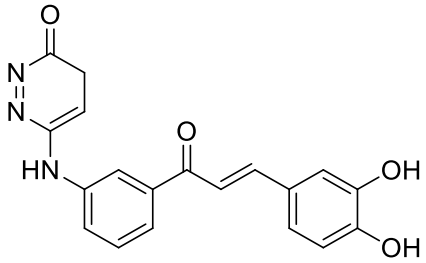
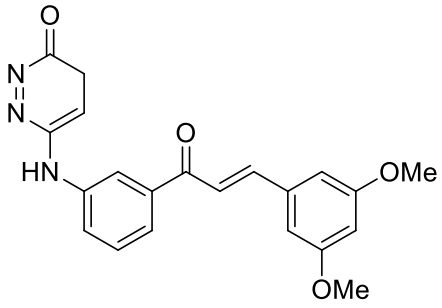
3k		75	3.5	161
3l		61	4	193
3m		60	4.5	183
3n		70	4	158
3o		85	4	190

Table 2 Antimicrobial Activity of Substituted Chalcones.

Entry	R	Bacteria		Fungi	
		E. Coli	S. aureus	Niger	• Albicans
		(ATCC 8739)	*(ATCC6538)*	(ATCC16404)	(ATCC10231)

3a	-H	12mm	10mm	-ve	10mm
3b	3,4-OCH_3	7mm	8mm	-ve	8mm
3c	4-OH	12mm	10mm	-ve	-ve
3d	2-OH	8mm	-ve	-ve	11mm
3e	3,4,5-Br,OCH_3,OH	10mm	6mm	-ve	9mm
3f	3-NO_2	9mm	7mm	10mm	10mm
3g	4-Cl	8mm	9mm	11mm	8mm
3h	4-NO_2	11mm	7mm	12mm	9mm
3i	4-OCH_3	11.5mm	9mm	-ve	11mm
3j	2-NO_2	10mm	9mm	-ve	13
3k	3, 4, 5-OCH_3	-ve	11mm	8.5mm	10.5mm
3l	3,4-OH	12.5mm	10mm	8.5mm	12mm
3m	4-F	9.5mm	8mm	10.5mm	10.5mm
3n	2,6-Cl	10.5mm	10.5mm	7.8mm	11.5mm
3o	2,4 OCH_3	12.5mm	C11.00mm	8.5mm	13.5
Penicilin		10.5mm	8.5mm	-	-
Griseofulvin		-	-	10.5mm	10mm

*Zone of inhibition in mm.

Conclusion

Chalcones, aromatic ketones and enones, are known for their microbial effects. Different varieties of Chalcone derivatives were synthesised and further used in synthesis of many heterocyclic compounds. The yield of substituted Chalcone derivatives by Green Chemistry (Microwave irradiation) method were found to be in the range of 65-85% All the synthesized compounds were purified by recrystallization and by column chromatography & was ascertained by melting point and TLC. The Synthesized Chalcones were further established by IR,1H NMR & Mass spectral studies. Based on spectral data, it was proved that all synthesized derivatives of chalcones meet the standard values of various spectral techniques. All the chalcone derivatives were evaluated for the above-mentioned microbial activities and they have exhibited promising activity. From above observation (**Table 2)**, it's clear that novel synthesized chalcones were microbial active.

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Conflicts of interest

No any conflict of interest.

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