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Research Article

Synthesis and antifungal activity of some new fluorinated 1-[2-hydroxyethyl] -3-ethoxycarbonyl-5 – oxadiazolyl/triazolyl/ pyrrolylaminocarbonylmethoxy-2- methylbenz [g] indoles

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ABSTRACT

The exclusive formation of 1-[2- aryl]-3-ethoxycarbonyl-7-halo-2-methylbenz [g] indol-5-yloxyacetic acid hydrazides (5a-c) from 1-[2-aryl]-3-ethoxycarbonyl – 5- hydroxy-7-halo-2-methylbenz [g] indoles (3a-c) revealed the chemo selectivity of the C_5 - ester over C_3-ester towards nucleophillic attack of hydrazine hydrate. This monocarbohydrazide (5a-c) is reacted separately with CS_2/KOH , acetonyl acetone and isothiocyanates to secure the desired 1-[2-aryl]-3-ethoxycarbonyl-5-(5-mercapto-1,3,4-oxadiazol-2-yl) methoxy-7-halo-2-methylbenz [g] indoles (8a-c), 1-[2-aryl]-3-ethoxycarbonyl-5-(2,5-dimethylpyrrol-1-yl) aminocarbonylmethoxy-7- halo-2-methylbenz [g] indoles (9a-c) and 1-[2-aryl]-3-ethoxycarbonyl-5-(aryl[1]substituted thiosemicarbazinocarbonyl) methoxy-7-halo -2- methylbenz [g] indoles (6a-i). These thiosemicarbazides (6a-i) are reacted with 4% NaOH to produce the 1-[2-aryl] 5-(4-aryl[1]subsituted-5-mercapto-1, 2, 4-triazol-3-yl) methoxy-7-halo -2- methylbenz [g] indole-3-carboxylic acid (7a-i).

Antifungal activity has been compared with Dithane M-45, a commercial fungicide for their fungi toxic action against Phytopthora infestans and Collectotricum falcatum, and the results correlated with their features.

Keywords: Chemo selectivity, Indole derivatives, fungicidal activity, pharmacological properties, infrared spectra, NMR Spectra.

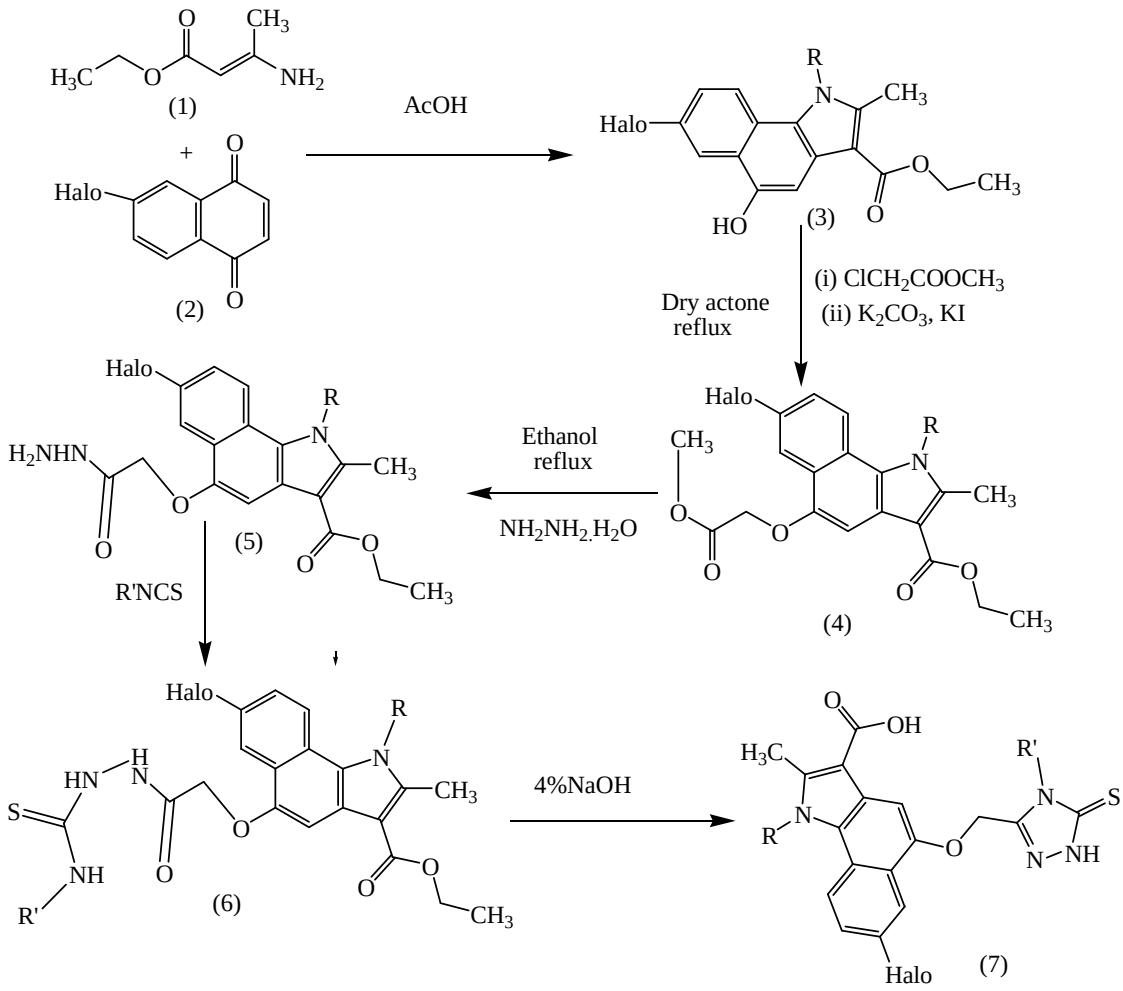
INTRODUCTION

Indole derivatives exhibited versatile pharmacological properties such as anticancer[1-4], antidepressant[5], antihypertensive[6], psychomimetic[7], antimicrobial[8], antidiabetic[9], antimalarial[10] and antiinflammatory[11-13]. Pyrroles[14, 15], oxadiazoles[16, 17] and triazoles have also displayed varied biodynamic properties. So far, synthesis of 5-hydroxy-7-halo-benz [g] indole carrying aryl group at the position – 1 is not reported. In the light of above reports and in continuation of the previous work ,we now report for the first time the synthesis of new 1-[2-aryl]-3-ethoxycarbonyl-5-hydroxy-7-halo-2-methylbenz [g] indoles (3a-c) which was converted into hitherto unknown bisheterocycles where in pyrroles, oxadiazoles and triazoles were linked to the C_5 – position of benz [g] indole nucleus via methylenoxy bridge.

The new 1-[2-aryl]-3-ethoxycarbonyl – 5- hydroxy-7-halo-2-methylbenz [g] indoles (3a-c) was prepared from 6-halo-1, 4-naphthoquinone 1 and N-[2-aryl]-β-amino crotonates (2a-c). This compound (3a-c) was reacted with methylchloroacetate in the presence of anhydrous K_2CO_3 and KI in refluxing dry acetone to obtain 1- [2-aryl] -3- ethoxycarbonyl-5-methoxycarbonyl- methoxy-7-halo-2-methylbenz [g] indoles (4a-c) and this benz [g] indole diester (4a-c) was further reacted with hydrazine hydrate in refluxing ethanol to yield only the monocarbohydrazide , 1-[2- aryl]-3-ethoxycarbonyl-7-halo-2- Methylbenz [g] indol-5-ylacetic acid hydrazides (**5a-c).**The C_5 ester group of the diester **(4a-c)** revealed chemo selectivity over the C_3 ester group towards the attack of hydrazine hydrate and thus produce monocarbohydrazide **(5a-c)**. This monocarbohydrazide **(5a-c)** was reacted separately with CS_2/KOH, acetonyl acetone and aryl[1]isothiocyanates to yield the desired 1-[2-aryl]-3-ethoxycarbonyl-5-(5-mercapto-1,3,4-oxadiazol-2-yl) methoxy-7-halo-2-methylbenz [g] indoles **(8a-c)**, 1-[2-aryl]-3-ethoxycarbonyl-5-(2,5-dimethylpyrrol-1-yl) aminocarbonylmethoxy-7-halo-2-methylbenz [g] indoles **(9a-c)** and 1-[2-aryl]-3-ethoxycarbonyl-5-(aryl[1] substituted thiosemicarbazinocarbonyl) methoxy-7-halo -2- methylbenz [g] indoles **(6a-i)** . These thiosemicarbazides **(6a-i)** were reacted with 4% NaOH to produce the 1-[2-aryl]-5-(4-aryl[1]subsituted-5-mercapto-1, 2, 4-triazol-3-yl) methoxy-7-halo -2- methylbenz [g] indole-3-carboxylic acid **(7a-i)**. The reaction sequence leading to the formation of the title compounds has been outlined in **Scheme No.1** and **Scheme No.2.**

EXPERIMENTAL

All melting points determined in the open glass capillaries. All the solvents and reagents used were of Analytical grade. All the reactions were monitored by TLC using benzene: methanol (9:2), Methylene dichloride: Ethyl acetate: Methanol (60: 35: 05) and Toluene: Ethyl acetate (7: 3) as solvent system. TLC



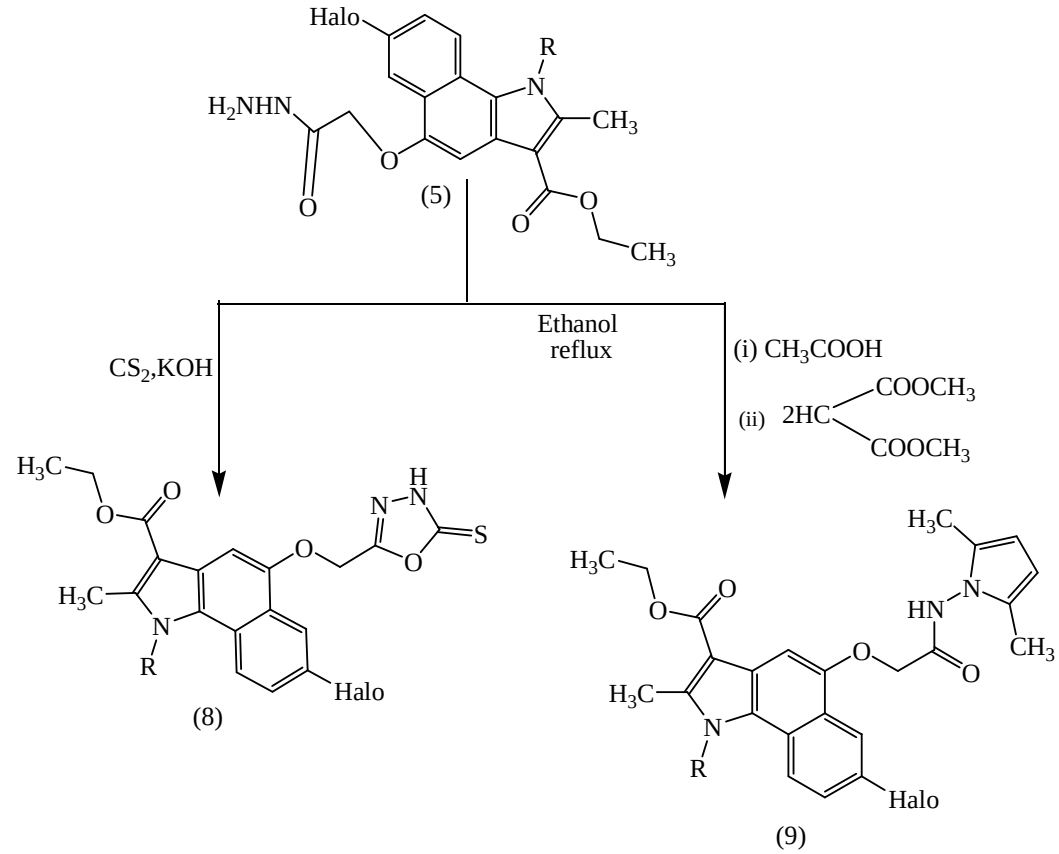
R= (a) C_2H_4OH: (b) C_6H_4OH : (c) 2-Cl-C_6H_3OH R'= (a, b , c) C_2H_4OH: (d,e,f,)C_6H_4OH :(g,h,i) 2-Cl-C_6H_3OH

Halo = a, b, c, d ,e, f, g, h ,i=F

Scheme No.1

plates were prepared by spreading method. These were dried in the air and then activated by heating in hot air oven at 110°C for 30 minutes Iodine vapors were used for visualization of TLC plates. IR spectra in KBr were recorded on Perkin-Elmer infrared spectrophotometer (λ max in cm^{-1}) and ^1H NMR spectra in DMSO-d_6 on EM-360L (60MHz) NMR Spectrometer using TMS as internal references (Chemical shifts in δ ppm) . All the compounds have given satisfactory elemental, analytical (C, H, N, and S) IR and ^1H NMR spectra.

1-[2-Aryl]-3-ethoxycarbonyl-5-hydroxy-7-halo-2-methylbenz [g] indoles (3): To the N-[aryl]-β-aminocrotonates **(2)** (0.05 M) in glacial acetic acid (100 mL) was added 6-halo-1, 4-naphthaquinone **(1)** (0.055 M) in small portions with continuous stirring. The mixture was heated at 50-60° C for 5-6 hrs and left overnight at room temperature. The solid thus separated was collected by filtration and recrystallized from suitable solvents. All the synthesized compounds with their characterization data as yield, melting point, molecular formulae, elemental analysis, recorded in **Table-2**.



R= (a) C_2H_4OH: (b) C_6H_4OH : (c) 2-Cl-C_6H_3OH R'= (a, b , c) C_2H_4OH: (d,e,f,)C_6H_4OH :(g,h,i) 2-Cl-C_6H_3OH

Halo = a, b, c, d ,e, f, g, h ,i=F

Scheme No.2

IR and ^{1}H NMR spectra of compound 3a: IR (KBr): 3370 (C_5-OH), 3240 (alcoholic-OH), 1653 (C_3-ester C=O) cm^{-1} .^{1}H NMR(DMSOd_6)δ:1.45(t,3H,C_3-ester CH_3) , 2.83(s,3H,C_2-CH_3), 3.95(t,2H,CH_2-O-),4.34 (q,2H,N-CH_2), 4.92(s,2H,-OCH_2),7.32-7.65(m, 2H, C_6 and C_8-H),7.75(s,1H,C_4-H),8.35 (d,1H,C_9-H),9.36(br,2H,C_5-OH and CH_2-OH, vanished on D_2O exchange).

1-[2-Aryl]-3-ethoxycarbonyl-5-methoxycarbonylmethoxy-7-halo-2-methyl Benz [g] indole (4): To 5-hydroxybenz [g] indoles **(3)** (0.03 M) in dry acetone (100mL) was added methyl chloroacetate (0.06 M), anhydrous potassium carbonate (8 g) and potassium iodide (0.1 g). The mixture was heated at reflux for 50 hrs. It was filtered hot and the solvent was removed under reduced pressure. The residue was recrystallized from suitable solvent. All the synthesized compounds are given in **Table-2** with their characterization data melting point, yield, molecular formula, elemental analysis..

IR and ^{1}H NMR spectra of compound 4a: IR (KBr): 3284 (alcoholic-OH), 1731 (C_5-ester C=O),1658 (C_3-ester C=O) cm^{-1} .^{1}H NMR(DMSO-d_6)δ: 1.50(t,3H, C_3-ester CH_3),2.85 (s,3H,C_2-CH_3),3.86 (s,3H

C_5-ester CH_3) 4.40(q,2H, C_3-ester CH_2), 4.51(t,2H CH_2-O-),4.90 (s,1H,-OH),7.23-7.64(m 5H, C_8-H and aromatic-H) , 7.71(s,1H,C_4-H) , 8.24 (d,1H,C_6-H), 8.54(d,1H,C_9-H)

1-[2- Aryl]-3-ethoxycarbonyl-7-halo-2-methylbenz [g] indol-5-yloxyacetic acid hydrazides(5):A mixture of Benz [g] indole dicarboxylate **(4)** (0.01 M) in ethanol (50 mL), hydrazine hydrate (99%) (0.02 M) and pyridine (2 drops) was heated on a boiling water bath for 20 hrs and concentrated to half volume and left overnight. The separated solid was filtered, washed with little ethanol and recrystallized from suitable solvent. All the synthesized compounds with their characterization data as yield, melting point, molecular formulae, elemental analysis are recorded in **Table-2**.

IR and ^{1}H NMR spectra of compound 5a

IR (KBr):3302 (NH/NH_2 and alcoholic-OH) and 1673(C_5-amide C=O and C_3-ester C=O) cm^{-1} .
^{1}H NMR (DMSO-d_6)δ: 1.41(t,3H,C_3-ester CH_3) , 2.82(s,3H,C_2-CH_3), 3.85(q,2H CH_2-O-),4.35(q 2H, C_3-ester CH_2),4.40(br, 2H,NH_2,vanished on D_2O exchange),4.66(m,4H,C_3-OCH_2 and N-CH_2),5.10(t,1H,OH,disappeared on D_2O exchange),7.47-7.68(m,2H,C_8 and C_4-H), 8.38 (d,1H,C_6-H), 8.50(d,1H,C_9-H), 9.43(s,1H,NH, vanished on D_2O exchange).

IR and ^{1}H NMR spectra of compound 5c

IR (KBr):3308 (NH/NH_2 and alcoholic-OH) and 1671(C_5-amide C=O and C_3-ester C=O) cm^{-1}.
^{1}H NMR (DMSO-d_6)δ: 1.43(t,3H,C_3-ester CH_3) , 2.81(s,3H,C_2-CH_3), 3.87(q,2H CH_2-O-),4.37(q 2H, C_3-ester CH_2), 4.41(br,2H,NH_2,vanished on D_2O exchange),5.13(t, 1H,OH,disappeared on D_2O exchange), 7.41-7.79 (m 5H, C_8, C_4-H and aromatic-H),8.37 (d,1H,C_6-H),8.52(d,1H,C_9-H),9.41(s,1H,NH vanished on D_2O exchange).

1-[2-Aryl]-3-ethoxycarbonyl-5-(aryl^1 substituted thiosemicarbazino-carbonyl) methoxy-7-halo -2- methylbenz [g] indoles (6): To a solution of monocarbohydrazide **(5)** (0.005 M) in ethanol (50 mL) was added aryl^{1}substituted isothiocyanates (0.005 M) with continuous stirring. The mixture was heated under reflux for 4-5 hrs and part of the solvent was evaporated. The solid that separated on cooling to room temperature was filtered, washed with ethanol and recrystallized. All the synthesized compounds with their characterization data as yield, melting point, molecular formulae, elemental analysis, are recorded in **Table-2**.

IR and ^{1}H NMR spectra of compound 6a

IR (KBr):3370, 3160, 3141(NH/OH), 1696 and 1659(C_3-ester and C_5-amide carbonyls) cm^{-1}. ^{1}H NMR (DMSO-d_6)δ: 1.23(t,2H,NH-CH_2),1.43 (t,3H,C_3-ester CH_3), 2.82(s,3H,C_2-CH_3), 3.87(t,2H CH_2-O), 4.11(q,2H CH_2-O), 4.33 (q,2H,C_3-ester CH_2), 4.66(t,2H,NCH_2),5.10 (s,2H,OH vanished on D_2O exchange), 5.44(s,2H,OCH_2),7.49-7.61(m,1H,C_8-H),7.91(s,1H, C_4-H),8.25(d,1H,C_6-H),8.36 (d,1H,C_9-H),9.53,10.14 and 13.90 (s,3H,NH disappeared on D_2O exchange).

IR and ^{1}H NMR spectra of compound 6d

IR (KBr):3373, 3168, 3147(NH/OH), 1699 and 1664(C_3-ester and C_5-amide carbonyls) cm^{-1}.
^{1}H NMR (DMSO-d_6)δ: 1.48(t,3H,C_3-ester CH_3), 2.86(s,3H,C_2-CH_3), 3.89(t,2H, CH_2-O-),4.39 (q,2H,C_3-ester CH_2), 4.63(t,2H,NCH_2), 5.13 (s,2H,OH vanished on D_2O exchange), 5.48(s,2H,OCH_2),

7.31-7.89(m 5H, C_8-H and aromatic-H), 7.91 (s,1H, C_4-H), 8.27(d,1H,C_6-H) 8.38 (d,1H,C_9-H)9.48,10.18 and 13.91 (s,3H,NH, disappeared on D_2O exchange).

IR and ^{1}H NMR spectra of compound 6h

IR (KBr):3369, 3163, 3139(NH/OH), 1693 and 1656 (C_3-ester and C_5-amide carbonyls) cm^{-1}. ^{1}H NMR (DMSO-d_6)δ: 1.41(t,3H,C_3-ester CH_3), 2.83(s,3H,C_2-CH_3), 4.37 (q,2H,C_3-ester CH_2),5.18 (s,2H,OH vanished on D_2O exchange), 5.46(s,2H,OCH_2), 7.21-7.98(m 8H, C_8-H and aromatic-H), 7.93 (s,1H, C_4-H),8.23(d,1H,C_6-H), 8.39 (d,1H,C_9-H),9.46,10.17 and 13.93 (s,3H,NH, disappeared on D_2O exchange).

1-[2-Aryl] 5-(4-aryl^{1}subsituted-5-mercapto-1, 2, 4-triazol-3-yl) methoxy-7-halo -2- methylbenz [g] indole-3-carboxylic acid (7): The suspension of thiosemicarbazides **(6)** (0.001 M) in sodium hydroxide (4%, 10mL) was refluxed for about 5-6 hrs. The reaction mixture after cooling to room temperature was poured into crushed ice (20 g) and acidified carefully with dilute acetic acid. The precipitate thus obtained was filtered, washed with water, dried and recrystallized from suitable solvents. All the synthesized compounds with their characterization data as yield, melting point, molecular formulae, elemental analysis are recorded in **Table-3**.

IR and ^{1}H NMR spectra of compound 7a

IR (KBr): 3401 (OH/NH), 1641 (C_3-ester C=O), 1153(C=S) cm^{-1} .^{1}H NMR (DMSO-d_6)δ : 2.84(s,3H,C_2-CH_3),3.88(t,4H,CH_2-O),4.68(t,4H,2N-CH_2),5.10(br, 2H, OH vanished on D_2O exchange), 5.41(s,2H,OCH_2), 7.40-8.60(m,4H,Ar-H), 12.24(br,1H,C_3-COOH, disappeared on D_2O exchange) and 13.83(br,1H,triazole NH, vanished on D_2O exchange).

IR and ^{1}H NMR spectra of compound 7f

IR (KBr): 3405 (OH/NH), 1646 (C_3-ester C=O), 1156(C=S) cm^{-1}. ^{1}H NMR (DMSO-d_6)δ:2.89(s,3H,C_2-CH_3), 5.13(br, 2H, OH vanished on D_2O exchange), 5.46(s,2H,OCH_2), 7.23-8.82(m,11H,Ar-H), 12.31(br,1H,C_3-COOH, disappeared on D_2O exchange) and 13.86 (br,1H,triazole NH, vanished on D_2O exchange).

IR and ^{1}H NMR spectra of compound 7i

IR (KBr): 3407 (OH/NH), 1642 (C_3-ester C=O), 1157(C=S) cm^{-1}.^{1}H NMR (DMSO-d_6)δ:2.86(s,3H,C_2-CH_3), 5.11(br, 2H, OH vanished on D_2O exchange), 5.45(s,2H,OCH_2), 7.16-8.71(m,10H,Ar-H), 12.28(br,1H,C_3-COOH, disappeared on D_2O exchange) and 13.82 (br,1H,triazole NH, vanished on D_2O exchange).

1-[2-Aryl]-3-ethoxycarbonyl-5-(5-mercapto-1, 3, 4-oxadiazol-2-yl) methoxy-7-halo-2-methylbenz[g] indoles (8):A mixture of indole monocarbohydrazide **(5)** (0.0015 M) in ethanol (20 mL), potassium hydroxide (0.003 M) dissolved in water (3 mL) and carbon disulfide (0.0045 M) was heated under reflux until the evolution of hydrogen sulphide gas ceased (about 25 hrs). The reaction mixture was cooled to room temperature and poured into ice cold water (100mL). It was then neutralized with dilute hydrochloric acid. The precipitated solid was filtered, washed with water dried and recrystallized. All the synthesized compounds with their characterization data as yield, melting point, molecular formulae, elemental analysis are recorded in **Table-3**.

IR and ^{1}H NMR spectra of compound 8a

.IR (KBr): 3438 (NH/OH), 1652 (C_3-ester C=O), 1140(C=S) cm^{-1} .^{1}H NMR (DMSO-d_6)δ:1.40(t,3H,C_3-ester CH_3),2.79(s,3H,C_2-CH_3), 3.85(t,2H,CH_2-O), 4.31 (q,2H,C_3-ester CH_2),4.63(t,2H,N-CH_2),5.16(br, 1H, OH vanished on D_2O exchange), 5.44(s,2H,C_5-OCH_2), 7.48-7.66 (m,1H,C_8-H), 7.81(s,1H,C_4-H), 8.30(d,1H,C_6-H), 8.37(d,1H,C_9-H), 14.32 (br,1H,oxadiazole NH, disappeared on D_2O exchange).

IR and ^{1}H NMR spectra of compound 8b

IR (KBr): 3432 (NH/OH), 1647 (C_3-ester C=O), 1142(C=S) cm^{-1} .^{1}H NMR (DMSO-d_6)δ: 1.42 (t,3H,C_3-ester CH_3),2.81(s,3H,C_2-CH_3),4.32 (q,2H,C_3-ester CH_2), 5.13(br, 1H, OH vanished on D_2O exchange), 5.48(s,2H,C_5-OCH_2), 7.41-7.69 (m,5H,C_8-H and Ar-H), 7.83(s,1H,C_4-H), 8.36(d,1H,C_6-H), 8.39(d,1H,C_9-H), 14.38 (br,1H,oxadiazole NH, disappeared on D_2O exchange).

IR and ^{1}H NMR spectra of compound 8c

IR (KBr): 3442 (NH/OH), 1654 (C_3-ester C=O), 1156(C=S) cm^{-1} .^{1}H NMR (DMSO-d_6)δ: 1.46(t,3H,C_3-ester CH_3),2.84(s,3H,C_2-CH_3), 4.38 (q,2H,C_3-ester CH_2), 5.18(br, 1H, OH vanished on D_2O exchange), 5.52(s,2H,C_5-OCH_2), 7.20-7.83 (m,4H,C_8-H and Ar-H), 7.89(s,1H,C_4-H), 8.39(d,1H,C_6-H), 8.43(d,1H,C_9-H), 14.42 (br,1H,oxadiazole NH, disappeared on D_2O exchange).

1-[2-Aryl]-3-ethoxycarbonyl-5-(2, 5-dimethylpyrrol-1-yl) aminocarbonyl methoxy -7- halo-2-methylbenz [g] indoles (9)

To a suspension of monocarbohydrazide **(5)** (0.001 M) in ethanol (10 mL) was added acetonyl acetone (0.002 M) in glacial acetic acid (1 mL) and reaction mixture was heated on a boiling water bath for 4-5 hrs. The reaction mixture was concentrated to half of its original volume and poured into crushed ice (50 g). The separated solid was filtered, washed with water dried and recrystallized from suitable solvent. All the synthesized compounds with their characterization data as yield, melting point, molecular formulae, elemental analysis are recorded in **Table-3**.

IR and ^{1}H NMR spectra of compound 9a

IR (KBr):3462 and 3326(NH and OH), 1689 and 1671(C_3-ester and C_5-amide carbonyls) cm^{-1}.^{1}H NMR (DMSO-d_6)δ: 1.39(t,3H,C_3-ester CH_3),1.97(s,6H,pyrrol$^1_2$ and 5^1-CH_3), 2.83(s,3H,C_2-CH_3),3.88(t,2H,CH_2-O),4.32(q, 2H,C_3-ester CH_2),4.67(t,2H,N-CH_2), 4.99 (s,2H,C_5-OCH_2),5.13 (s, 1H, OH vanished on D_2O exchange),5.64(s,2H,C^1_3 and C^1_4-H of pyrroles),7.51-7.63 (m,1H,C_8-H),7.65(s,1H,C_4-H), 8.39(d,1H,C_6-H), 8.52(d,1H,C_9-H),11.08 (s,1H, NH, disappeared on D_2O exchange).

IR and ^{1}H NMR spectra of compound 9b

IR (KBr):3469 and 3329(NH and OH), 1693 and 1673(C_3-ester and C_5-amide carbonyls) cm^{-1} .^{1}H NMR (DMSO-d_6)δ: 1.36(t,3H,C_3-ester CH_3),1.99(s,6H, pyrrol$^1_2$ and 5^1-CH_3), 2.87(s,3H,C_2-CH_3), 4.38(q,2H,C_3-ester CH_2), 4.97(s,2H,C_5-OCH_2),5.16 (s, 1H, OH vanished on D_2O exchange),5.69(s,2H, C^1_3 and C^1_4-H of pyrroles),7.56-7.81 (m,5H,C_8-H and Ar-H), 7.61(s,1H,C_4-H), 8.42(d,1H,C_6-H), 8.54(d,1H,C_9-H),11.09 (s,1H, NH, disappeared on D_2O exchange).

IR and ^{1}H NMR spectra of compound 9c

IR (KBr):3466 and 3328(NH and OH), 1691 and 1671(C_3-ester and C_5-amide carbonyls) cm^{-1} .
^{1}H NMR (DMSO-d_6)δ 1.43(t,3H, C_3-ester CH_3),2.02 (s, 6H, pyrrol$^1_2$ and 5^1-CH_3),2.90(s,3H,C_2-CH_3), 4.40(q,2H,C_3-ester CH_2), 5.01(s,2H,C_5-OCH_2),5.19 (s, 1H, OH vanished on D_2O exchange),5.73 (s,2H, C^1_3 and C^1_4-H of pyrroles),7.21-7.63 (m, 4H,C_8-H and Ar-H),7.63 (s,1H,C_4-H), 8.44(d,1H,C_6-H), 8.59(d,1H,C_9-H),11.11 (s,1H, NH, disappeared on D_2O exchange).

FUNGICIDAL ACTIVITY

The fungicidal activity of the compounds **(7a-i)**, **(8a-c)** and **(9a-c)** were evaluated against ***Phytopthora infestans*** and ***Collectotricum falcatum*** by the usual agar plate techniques[18] at 1000, 100 and 10 ppm concentrations[19-23]. **Dithane M-45** standard commercial fungicide was also tested under similar conditions for comparison. The antifungal activity results of the compounds **(7a-i)**, **(8a-c)** and **(9a-c)** are summarized in **Table-1.**

RESULT AND DISCUSSIONS

The new indole compound (3a-c) was prepared from crotonates (2a-c). This compound (3a-c) was reacted with methylchloroacetate in the presence of anhydrous K_2CO_3 and KI in refluxing dry acetone to obtain methylbenz [g] indoles diester (4a-c) and this methylbenz [g] indole diester (4a-c) was further reacted with hydrazine hydrate in refluxing ethanol to yield only the monocarbohydrazide (**5a-c)**.The C_5 ester group of the diester **(4a-c)** revealed chemo selectivity over the C_3 ester group towards the attack of hydrazine hydrate and thus produce monocarbohydrazide **(5a-c)**. This monocarbohydrazide **(5a-c)** was reacted separately with CS_2/KOH, acetonyl acetone and aryl^{1}isothiocyanates to yield the desired indoles **(8a-c)**, **(9a-c)** and thiosemicarbazides **(6a-i)**. These thiosemicarbazides **(6a-i)** were reacted with 4% NaOH to produce the 1-[2-aryl]-5-(4-aryl^{1}subsituted-5-mercapto-1, 2, 4-triazol-3-yl) methoxy-7-halo -2- methylbenz [g] indole-3-carboxylic acid **(7a-i)**. The structures of the compounds were confirmed by their Melting points, elemental analysis, IR bands and position in ^{1}H NMR spectra.

CONCLUSION

It appeared from screening results that most of the compounds **(7a-i),(8a-c)** and **(9a-c)** significantly inhibited the mycelia growth of both test fungi at 1000 ppm but their activity decreased considerably at lower concentrations (100 and 10ppm). The compounds **7c, 7e, 7f, 7i**, 8c and **9c** had similar activity at 1000 ppm and showed **54-46%** growth inhibition of both test fungi at 10 ppm concentration. Significant alteration of the fungicidal activity was observed with the change in the relative position of the substituent on triazoles,oxadiazoles and dimethylpyrroles with indoles ring e.g. compounds **7c, 7f, 7i, 8c** and **9c** bearing chlorophenol group were found to be more active than **7b, 7d, 7e, 7h, 8b** and **9b** phenol groups. Likewise, introduction of the chloro group was more effective than that at phenyl group.

Table 1: Antifungal Activity data of 1-[2-aryl] 5-(4-aryl[1]subsituted-5-mercapto-1,2,4-triazol-3-yl) methoxy-7-halo -2- methylbenz [g] indole-3-carboxylic acids (7a-i) , 1-[2-aryl]-3-ethoxycar- bonyl-5-(5-mercapto-1,3,4-oxadiazol-2-yl) methoxy-7-halo-2-methylbenz [g] indoles (8a-c), and 1-[2-aryl]-3-ethoxycarbonyl-5-(2,5-dimethylpyrrol-1-yl)aminocarbon-ylmethoxy-7-halo-2-methylbenz[g] indoles (9a-c).

Compd. No.	Average % inhibition Against					
	Phytophthora Infestance at			*Collectotricum falcatum* at		
	1000 ppm	100 ppm	10 ppm	1000 ppm	100 ppm	10 ppm
7. a	93	60	43	92	59	40
b	96	62	50	95	60	43
c	99	64	48	98	63	46
d	93	60	40	92	58	39
e	98	67	50	98	65	49
f	99	68	53	99	66	52
g	95	58	37	95	56	36
h	98	65	51	98	62	47
i	99	69	54	99	68	53
8.a	90	58	41	90	56	37
b	97	58	40	96	57	39
c	99	67	51	99	65	48
9.a	92	59	42	90	58	40
b	97	62	50	97	60	46
c	99	64	51	99	67	49
Dithane M-45	**100**	**85**	**69**	**100**	**84**	**67**

Table 2: Characterization data of 1-[2-aryl]-3-ethoxycarbonyl–5- hydroxy-7-halo-2-methylbenz [g] indoles (3a-c), 1- [2-aryl] -3- ethoxycarbonylmethoxy -7-halo-2- methylbenz [g] indoles (4a-c) , 1-[2-aryl]-3-ethoxycarbonyl-7-halo-2-methylbenz [g] indole-5-ylacetic acid hydrazides (5a-c) ,1-[2-aryl]-3-ethoxycarbonyl-5-(aryl[1] substituted thiosemicarbazinocarbonyl) methoxy-7-halo -2- methylbenz [g] indoles (6a-i)

Compd. No.	R	R^1	Molecular Formula	Melting point (^OC)	Yield (%)	Found (Calcd.) %			
						C	N	H	S
3a*	C_2H_4OH		$C_{18}H_{18}NO_4F$	262	58	62.21(65.25)	04.21(04.22)	05.46(04.43)	-
b	C_6H_4OH		$C_{22}H_{18}NO_4F$	268	55	69.63(69.65)	03.71(03.69)	04.72(04.74)	-
c	o-ClC_6H_3OH		$C_{22}H_{17}NO_4FCl$	259	57	63.86(63.84)	03.36(03.38)	04.10(04.11)	-
4a	C_2H_4OH		$C_{21}H_{22}NO_6F$	142	78	62.54(62.53)	03.45(03.47)	05.46(05.45)	-
b*	C_6H_4OH		$C_{25}H_{22}NO_6F$	147	79	66.50(66.51)	03.09(03.10)	04.88(04.87)	-
c	o-ClC_6H_3OH		$C_{25}H_{21}NO_6FCl$	145	80	61.80(61.79)	02.87(02.88)	04.33(04.32)	-
5a*	C_2H_4OH		$C_{20}H_{22}N_3O_5F$	262	52	59.53(59.55)	10.41(10.42)	05.46(05.45)	-
b	C_6H_4OH		$C_{24}H_{22}N_3O_5F$	264	51	63.86(63.85)	09.30(09.31)	04.85(04.87)	-
c*	o-ClC_6H_3OH		$C_{24}H_{21}N_3O_5FCl$	265	52	59.33(59.32)	08.66(08.65)	04.34(04.32)	-
6a*	C_2H_4OH	C_2H_4OH	$C_{23}H_{27}N_4O_6FS$	230	72	54.55(54.54)	11.08(11.06)	05.36(05.33)	06.33(06.32)
b	C_6H_4OH	C_2H_4OH	$C_{27}H_{27}N_4O_6FS$	222	71	58.46(58.48)	10.11(10.10)	04.89(04.87)	05.79(05.77)
c	o-ClC_6H_3OH	C_2H_4OH	$C_{27}H_{26}N_4O_6FSCl$	227	70	55.08(55.05)	09.54(09.51)	04.40(04.41)	05.42(05.43)
d*	C_2H_4OH	C_6H_4OH	$C_{27}H_{27}N_4O_6FS$	226	73	58.50(58.48)	10.12(10.10)	04.86(04.87)	05.74(05.77)
e	C_6H_4OH	C_6H_4OH	$C_{31}H_{27}N_4O_6FS$	228	71	61.81(61.79)	09.32(09.30)	04.50(04.48)	05.30(05.31)
f	o-ClC_6H_3OH	C_6H_4OH	$C_{31}H_{26}N_4O_6FSCl$	224	72	58.46(58.44)	08.80(08.79)	04.10(04.08)	05.04(05.02)
g	C_2H_4OH	o-ClC_6H_3OH	$C_{27}H_{26}N_4O_6FSCl$	223	70	55.09(55.05)	09.50(09.51)	04.43(04.41)	05.44(05.43)
h*	C_6H_4OH	o-ClC_6H_3OH	$C_{31}H_{26}N_4O_6FSCl$	226	72	58.46(58.44)	08.81(08.79)	04.09(04.08)	05.04(05.02)
i	o-ClC_6H_3OH	o-ClC_6H_3OH	$C_{31}H_{25}N_4O_6FSCl_2$	227	73	58.52(58.53)	08.83(08.81)	03.91(03.93)	05.01(05.03)

Table 3: Characterization data of 1-[2-aryl] 5-(4-aryl'subsituted-5-mercapto-1,2,4-triazol-3-yl) methoxy-7-halo-2- methylbenz [g] indole-3-carboxylic acid (7a-i) , 1-[2-aryl]-3-ethoxycarbonyl-5-(5-mercapto-1,3,4-oxadiazol-2-yl) methoxy-7-halo-2-methylbenz [g] indoles(8a-c),and1-[2-aryl]-3ethoxycarbonyl-5-(2,5-dimethylpyrrol-1-l)aminocarbonylmethoxy-7-halo-2-methylbenz [g] indoles (9a-c).

Compd. No.	R	R^1	Molecular Formula	Melting point (^OC)	Yield (%)	Found (Calcd.) %			
						C	N	H	S
7a*	C_2H_4OH	C_2H_4OH	$C_{21}H_{21}N_4O_5FS$	218	65	54.76(54.78)	12.15(12.17)	04.57(04.56)	06.98(06.95)
b	C_6H_4OH	C_2H_4OH	$C_{25}H_{21}N_4O_5FS$	220	64	59.09(59.05)	11.06(11.02)	04.16(04.13)	06.31(06.29)
c	o-ClC_6H_3OH	C_2H_4OH	$C_{25}H_{20}N_4O_5FSCl$	217	63	55.32(55.29)	10.36(10.32)	03.64(03.68)	05.91(05.89)
d	C_2H_4OH	C_6H_4OH	$C_{25}H_{21}N_4O_5FS$	215	62	59.02(59.05)	11.04(11.02)	04.15(04.13)	06.31(06.29)
e	C_6H_4OH	C_6H_4OH	$C_{29}H_{21}N_4O_5FS$	213	64	62.56(62.58)	10.09(10.07)	03.76(03.77)	05.73(05.75)
f*	o-ClC_6H_3OH	C_6H_4OH	$C_{29}H_{20}N_4O_5FSCl$	217	63	58.90(58.93)	09.52(09.48)	03.36(03.38)	05.40(05.41)
g	C_2H_4OH	o-ClC_6H_3OH	$C_{25}H_{20}N_4O_5FSCl$	218	59	55.31(55.29)	10.34(10.32)	03.69(03.68)	05.86(05.89)
h	C_6H_4OH	o-ClC_6H_3OH	$C_{29}H_{20}N_4O_5FSCl$	215	58	58.91(58.93)	09.52(09.48)	03.41(03.38)	05.43(05.41)
i*	o-ClC_6H_3OH	o-ClC_6H_3OH	$C_{29}H_{19}N_4O_5FSCl_2$	216	61	55.64(55.68)	08.94(08.96)	03.06(03.04)	05.13(05.12)
8a*	C_2H_4OH	-	$C_{21}H_{20}N_3O_5FS$	246	63	56.64(56.62)	09.40(09.43)	04.52(04.49)	07.21(07.19)
b*	C_6H_4OH	-	$C_{25}H_{20}N_3O_5FS$	244	62	60.88(60.85)	08.56(08.51)	04.06(04.05)	06.47(06.49)
c*	o-ClC_6H_3OH	-	$C_{25}H_{19}N_3O_5FSCl$	245	61	56.81(56.87)	07.94(07.96)	03.63(03.60)	06.09(06.06)
9a*	C_2H_4OH	-	$C_{26}H_{28}N_3O_5F$	250	72	64.85(64.86)	08.71(08.73)	05.84(05.82)	-
b*	C_6H_4OH	-	$C_{30}H_{28}N_3O_5F$	251	74	68.08(68.05)	07.96(07.93)	05.26(05.29)	-
c*	o-ClC_6H_3OH	-	$C_{30}H_{27}N_3O_5FCl$	249	73	63.84(63.88)	07.48(07.45)	04.82(04.79)	-

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