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Synthesis and Evaluation of New 3-Substituted[3,4-dihydro pyrimidinones]indolin-2-ones for Antioxidant Activity

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New 3-substituted[3,4-dihydropyrimidinones]indolin-2-ones have been synthesized and tested for antioxidant activity by UV spectrophotometer and HPLC method. Among them compounds C_{16}, C_{15}, C_{14}, C_{13} and C_{12} exhibited higher antioxidant activity. However, these antioxidant activities are lower than ascorbic acid. Antioxidant activities are performed both UV-Vis spectrometer and reverse phase HPLC methods, both the methods were compared and found 2 to 5 % variation were observed. HPLC method is more sensitive and suitable for the said compounds than UV-Vis spectrometer.

Key Words: Synthesis, 3,4-Dihydro pyrimidinones, Antioxidant activity.

INTRODUCTION

Heterocyclic systems possessing an indole moiety exhibit a number of interesting biological activities such as antiviral, antibacterial, antifungal, antiinflammatory, analgesic, diuretic and anticonvulsant activities[1-8]. A lot of work has been carried out on indole derivatives and no work has been carried on 3-substituted[3,4-dihydro pyrimidinones]indolin-2-ones. It is also evident from the literature that dihydro pyrimidinones are equally important interms of pharmacological activities such as calcium channel blockers, antifungal and antihypertensive agents[9-11]. Therefore, it seemed promising to synthesize some new 3-substituted[3,4-dihydro pyrimidinones]-indolin-2-ones using the multi component one pot condensation of biginelli's synthesis using isatin semicarbazone, ethylacetoacetate and aromatic aldehyde[12]. Herein, the design of new 3-substituted[3,4-dihydro pyrimidinones]indolin-2-ones emphasizing in particular the presence of aromatic nucleus at the 5-postion of 3,4-dihydropyrimidine ring [benzaldehyde, 4-chlorobenzaldehyde, 4-hydroxybenzaldehyde and 4-methoxybenzaldehyde] in one skeleton (B_1 to B_9, C_1 to C_{36}, **Scheme-I**) are reported. All the compounds presented here were assayed for antioxidant activity by DPPH method using UV double beam spectrophotometer and reverse phase HPLC methods.

EXPERIMENTAL

All reagents used were purchased from SD Fine Chemical Company, Mumbai, India. Melting points were determined in an open capillaries on a galen camp apparatus (Sanyo gallen camp, lough, borough, UK) and were uncorrected. IR spectra (KBR, cm^{-1}) were recorded on Perkin-Elmer spectrophotometer (577 model). ^1H NMR spectra were recorded on a brukar WM-400 spectrophotometry (δ ppm).

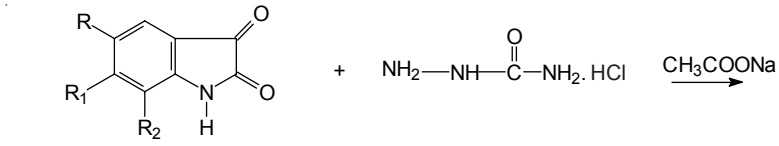
Isatin semicarbazone (B_1 to B_9): To a stirred solution of an appropriate isatin (A_1 to A_9) 2 g in 20 mL of alcohol at room temperature, semicarbazide hydrochloride, sodium acetate dissolved in water is added to the above solution and refluxed on a water bath for about 1 h. The resultant yellow crystalline solid was filtered, washed repeatedly with small portions of cold water and finally with small portions of cold methanol and recrystallized with methanol to give pure products (B_1 to B_9). The data of the compounds produced was compared with data available in the literature.

3-Substituted[3,4-dihydro pyrimidinones]indolin-2-ones (C_1 to C_{36}): Compounds B_1 to B_9 (2.04 g, 0.01 mol), ethylacetoacetate and aromatic aldehyde (0.01 mol), in dry methanol and a few drops of concentrated hydrochloric acid as a catalyst was condensed by multicomponent one pot condensation by named Biginelli's reaction for 10 to 12 h on a water bath. The solvent was evaporated, the precipitated solid was poured on to crushed ice, filtered, dried and recrystallized from methanol to give pure products (C_1 to C_{36}). The compounds obtained were characterized by physical and spectral data *e.g.*, the yield of the compound C_2[R_1=H, R_2=H, R_3=benzaldehyde] was 2 g [65] m.p. 246 ºC and spectral data (KBr): 1590 [NH, indole], 3330 [NH, pyrimidine], 1720 [NH-CO], 1688 [C=O, indole], 1621 [C=N, 1360-1280] [C-N,1300-1000 [C-O]. PMR spectra [DMSO-d_6, ppm] 12.03 [S, 1H, NH indole], 11.73 [S, 1H, NH pyrimidine] 6.0-7.0 [m, 8H, 2Ar-H], 0.9 [t-CH_3] 4.0 [q, 2H, O CH_2] 2.20 [S, 3H, CH_3] compounds C_{1-36} were prepared similarly.

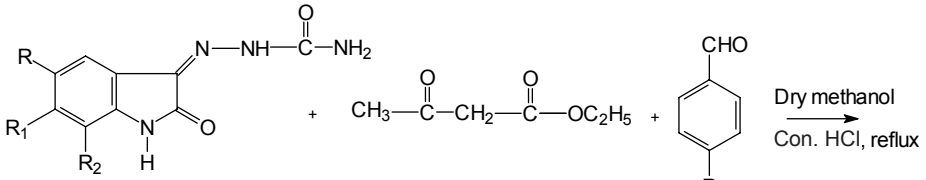
RESULTS AND DISCUSSION

The reaction sequence used in the synthesis of the target compounds C_{1-36} is depicted in the **Scheme-I**. Isatin semicarbazone B_{1-9} were obtained from appropriate isatin in alcohol with addition of semicarbazide hydrochloride and sodium acetate in water and refluxed on water-bath for *ca.* 1 h[13]. Compounds C_{1-36} were synthesized by refluxing B_{1-9} with ethylacetoacetate and an appropriate aromatic aldehydes (benzaldehyde, 4-chlorobenzaldehyde, 4-hydroxybenzaldehyde and 4-methoxybenzaldehyde by multi-component one pot condensation using named biginell's reaction in presence of catalytic amount of concentrated hydrochloric acid for 10-12 h[14]. All the newly synthesized compounds were characterized by physical, spectral (IR, Mass, NMR) and elemental analysis.

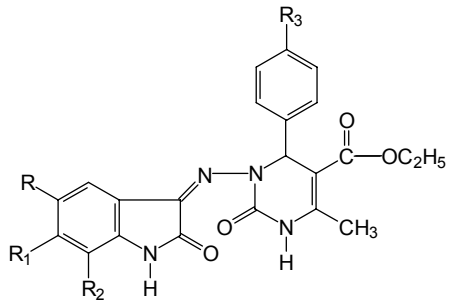
Antioxidant activity by DPPH method by UV: Antioxidant activity is carried out by using the DPPH (diphenylpicryl hydrazyl) method[15] using UV spectrophotometer. The methanolic solution of 0.2 mM of DPPH is used for the estimation.



(A_1 to A_9)



(B_1 to B_9)



(C_1 to C_{36})

R = H, CH_3, F, Cl, Br

R_1 = Br

R_2 = Br, Cl, CH_3

R_3 = Benzaldehyde, 4-Cl benzaldehyde, 4-OH benzaldehyde, 4-OCH_3 benzaldehyde

Legends to **Scheme-I**

A_1, B_1: R = H, R_1 = H, R_2=H

A_2, B_2: R = CH_3, R_1=H, R_2=H

A_3, B_3: R = F, R_1= H, R_2=H

A_4, B_4: R = Cl, R_1= H, R_2=H

A_5, B_5: R = Br, R_1= H, R_2=H

A_6, B_6: R = H, R_1= Br, R_2=H

A_7, B_7: R = Br, R_1= H, R_2= Br

A_8, B_8: R = H, R_1= H, R_2= CH_3

A_9, B_9: R = H, R_1= H, R_2= Cl

C_1: R = H, R_1= H, R_2=H, R_3=C_7H_9O (Benzaldehyde)

C_2: R = CH_3, R_1= H, R_2=H, R_3=C_7H_9O (Benzaldehyde)

C_3: R = F, R_1= H, R_2=H, R_3=C_7H_9O (Benzaldehyde)

C_4: R = Cl, R_1= H, R_2=H, R_3=C_7H_9O (Benzaldehyde)

C_5: R = Br, R_1= H, R_2=H, R_3=C_7H_9O (Benzaldehyde)

C_6: R = H, R_1= Br, R_2=H, R_3=C_7H_9O (Benzaldehyde)

C_7: R = BR, R_1= H, R_2=BR, R_3=C_7H_9O (Benzaldehyde)

C_8: R = H, R_1= H, R_2=CH_3, R_3=C_7H_9O (Benzaldehyde)
C_9: R = H, R_1= H, R_2=Cl, R_3=C_7H_9O (Benzaldehyde)
C_{10}: R = H, R_1= H, R_2=H, R_3=C_7H_5OCl (4-Chloro benzaldehyde)
C_{11}: R = CH_3, R1= H, R_2=H, R_3=C_7H_5OCl (4-Chloro benzaldehyde)
C_{12}: R = F, R_1= H, R_2=H, R_3=C_7H_5OCl (4-Chloro benzaldehyde)
C_{13}: R = Cl, R_1= H, R_2=H, R_3=C_7H_5OCl (4-Chloro benzaldehyde)
C_{14}: R = Br, R_1= H, R_2=H, R_3=C_7H_5OCl (4-Chloro benzaldehyde)
C_{15}: R = H, R_1= Br, R_2=H, R_3=C_7H_5OCl (4-Chloro benzaldehyde)
C_{16}: R = Br, R_1= H, R_2=Br, R_3=C_7H_5OCl (4-Chloro benzaldehyde)
C_{17}: R = H, R_1= H, R_2=CH_3, R_3=C_7H_5OCl (4-Chloro benzaldehyde)
C_{18}: R = H, R_1= H, R_2=CL, R_3=C_7H_5OCl (4-Chloro benzaldehyde)
C_{19}: R = H, R_1= H, R_2=H, R_3=C_7H_6O (4-Hydroxy benzaldehyde)
C_{20}: R = CH_3, R_1= H, R_2=H, R_3=C_7H_6O (4-Hydroxy benzaldehyde)
C_{21}: R = F, R_1= H, R_2=H, R_3=C_7H_6O (4-Hydroxy benzaldehyde)
C_{22}: R = Cl, R_1= H, R_2=H, R_3=C_7H_6O (4-Hydroxy benzaldehyde)
C_{23}: R = Br, R_1= H, R_2=H, R_3=C_7H_6O (4-Hydroxy benzaldehyde)
C_{24}: R = H, R_1= Br, R_2=H, R_3=C_7H_6O (4-Hydroxy benzaldehyde)
C_{25}: R = Br, R_1= H, R_2=Br, R_3=C_7H_6O (4-Hydroxy benzaldehyde)
C_{26}: R = H, R_1= H, R_2=CH_3, R_3=C_7H_6O (4-Hydroxy benzaldehyde)
C_{27}: R = H, R_1= H, R_2=Cl, R_3=C_7H_6O (4-Hydroxy benzaldehyde)
C_{28}: R = H, R_1= H, R_2=H, R_3=$C_8H_8O_2$ (4-Methoxy benzaldehyde)
C_{29}: R = CH_3, R_1= H, R_2=H, R_3=$C_8H_8O_2$ (4-Methoxy benzaldehyde)
C_{30}: R = F, R_1= H, R_2=H, R_3=$C_8H_8O_2$ (4-Methoxy benzaldehyde)
C_{31}: R = Cl, R_1= H, R_2=H, R_3=$C_8H_8O_2$ (4-Methoxy benzaldehyde)
C_{32}: R = Br, R_1= H, R_2=H, R_3=$C_8H_8O_2$ (4-Methoxy benzaldehyde)
C_{33}: R = H, R_1= Br, R_2=H, R_3=$C_8H_8O_2$ (4-Methoxy benzaldehyde)
C_{34}: R = Br, R_1= H, R_2=Br, R_3=$C_8H_8O_2$ (4-Methoxy benzaldehyde)
C_{35}: R = H, R_1= H, R_2=CH_3, R_3=$C_8H_8O_2$ (4-Methoxy benzaldehyde)
C_{36}: R = H, R_1= H, R_2=Cl, R_3=$C_8H_8O_2$ (4-Methoxy benzaldehyde)

Scheme-I: Schematic diagram of 3-substituted[3,4-dihydro pyrimidinones]-indolin-2-ones

Required amount of test compounds was dissolved in methanol and 1 mM stock solution was prepared. Solutions of concentrations ranging from 100 mM to 1 mM were prepared from the stock solution. 0.2 mL of DPPH solution was added to 2.8 mL of ascorbic acid solution in a test tube wrapped with aluminum foil and its absorbance was read at 517 nm using UV-visible double beam spectrophotometer. The results were plotted on a graph and IC_{50} value was determined. All test compounds C_1 to C_{36} were determined by a procedure similar to the ascorbic acid determination.

Antioxidant activity by HPLC: Antioxidant activity of test compounds C_1 to C_{36}, were estimated by HPLC method. 0.2 mM DPPH in methanol by the same procedure of spectrophotometer described above and then subjected to a reversed phase HPLC analysis[16,17]. The HPLC equipment consisted of a Shimadzu LC1020 pump, Rheodyne injector fitted with a 20 µL loop and a Shimadzu SPD-10AV, UV-Vis detector set at 517 nm. Analysis were performed by Altech, ODS column (4.6 mm × 150 mm, India) at ambient temperature with a mobile phase of methanol/water (70:30, v/v) at a flow rate of 1 mL/min. The DPPH radical scavenging activity was

TABLE-1
PHYSICAL AND SPECTRAL DATA FOR 3-SUBSTITUTED[3,4-DIHYDROPYRIMIDINONES]INDOLIN-2-ONES

Compd.	R/ R_1/ R_2/ R_3	m.f. / m.p. (ºC)	Mass spectra / ^{1}H NMR	IC_{50} value (µM)	
				UV Method	HPLC method
C_1	H H H H	$C_{22}H_{20}N_4O_4$ 243	405, 11.70 [S, 1H, NH indole] 11.25 [S, 1H, NH pyrimidine] 6.6-7.6 [m, 9H, 2Ar-H] 0.9 [t, CH_3], 2.25 [S, 3H, CH_3], 4 [q, 2H, $0CH_2$]	32.53	31.01
C_2	CH_3 H H H	$C_{23}H_{22}N_4O_4$ 246	12.03 [S, 1H, NH indole] 11.73 [S, 1H, NH pyrimidine] 6.0-7.0 [m, 8H, 2Ar-H] 0.9 [t, CH_3], 2.25 [S, 3H, CH_3], 4 [q, 2H, $0CH_2$]	29.99	27.67
C_3	F H H H	$C_{22}H_{19}N_4O_4F$ 248	11.75 [S, 1H, NH indole] 11.50 [S, 1H, NH pyrimidine] 6.1-7.2 [m, 8H, 2Ar-H] 0.9 [t, CH_3], 2.20 [S, 3H, CH_3], 4 [q, 2H, $0CH_2$]	28.12	26.89
C_4	Cl H H H	$C_{22}H_{19}N_4O_4C1$ 251	11.75 [S, 1H, NH indole] 11.50 [S, 1H, NH pyrimidine] 6.1-7.2 [m, 8H, 2Ar-H] 0.9 [t, CH_3], 2.20 [S, 3H, CH_3], 4 [q, 2H, $0CH_2$]	25.90	23.76
C_5	Br H H H	$C_{22}H_{19}N_4O_4Br$ 252	11.75 [S, 1H, NH indole] 11.50 [S, 1H, NH pyrimidine] 6.1-7.2 [m, 8H, 2Ar-H] 0.9 [t, CH_3], 2.20 [S, 3H, CH_3], 4 [q, 2H, 0CH2]	21.03	19.75
C_6	H Br H H	$C_{22}H_{19}N_4O_4Br$ 253	11.75 [S, 1H, NH indole] 11.50 [S, 1H, NH pyrimidine] 6.0-7.2 [m, 8H, 2Ar-H] 0.9 [t, CH_3], 2.20 [S, 3H, CH_3], 4 [q, 2H, $0CH_2$]	22.58	21.02
C_7	Br H Br H	$C_{22}H_{18}N_4O_4Br_2$ 255	11.50 [S, 1H, NH indole] 11.25 [S, 1H, NH pyrimidine] 6.0-7.2 [m, 6H, 2Ar-H] 0.9 [t, CH_3], 2.20 [S, 3H, CH_3], 4 [q, 2H, $0CH_2$]	19.53	17.91
C_8	H H CH_3 H	$C_{23}H_{22}N_4O_4$ 244	12.0 [S, 1H, NH indole] 11.70 [S, 1H, NH pyrimidine] 6.0-7.0 [m, 8H, 2Ar-H] 0.9 [t, CH_3], 2.25 [S, 3H, CH_3], 3.9 [q, 2H, $0CH_2$]	31.20	30.17
C_9	H H C1 H	$C_{22}H_{19}N_4O_4C1$ 245	439.5, 11.70 [S, 1H, NH indole] 11.55 [S, 1H, NH pyrimidine] 6.6-7.6 [m, 8H, 2Ar-H] 0.9 [t, CH_3], 2.19 [S, 3H, CH_3], 4.2 [q, 2H, $0CH_2$]	27.03	26.05
C_{10}	H H H C1	$C_{22}H_{19}N_4O_4C1$ 244	439.5, 11.20 [S, 1H, NH indole] 10.80 [S, 1H, NH pyrimidine] 6.3-7.2 [m, 7H, 2Ar-H] 0.9 [t, CH_3], 2.50 [S, 3H, CH_3], 3.9 [q, 2H, $0CH_2$]	22.53	21.65
C_{11}	CH_3 H H C1	$C_{23}H_{20}N_4O_4C1$ 246	11.18 [S, 1H, NH indole] 10.88 [S, 1H, NH pyrimidine] 6.8-7.8 [m, 6H, 2Ar-H] 1.9 [t, CH_3], 2.6 [S, 3H, CH_3], 3.8 [q, 2H, 0CH2]	20.22	18.98

C_{12}	F H H C1	$C_{22}H_{18}N_4O_4C1F$ 248	10.99 [S, 1H, NH indole] 10.80 [S, 1H, NH pyrimidine] 6.6-7.6 [m, 6H, 2Ar-H] 0.8 [t, CH_3], 2.53 [S, 3H, CH_3], 3.8 [q, 2H, $0CH_2$]	16.40	15.11
C_{13}	Cl H H C1	$C_{22}H_{18}N_{4254}O_4C1_2$ 254	10.99 [S, 1H, NH indole] 10.80 [S, 1H, NH pyrimidine] 6.6-7.6 [m, 9H, 2Ar-H], 2.53 [S, 3H, CH_3], 0.9 [t, CH_3], 3.9 [q, 2H, OCH_2]	14.50	13.44
C_{14}	Br H H C1	$C_{22}H_{18}N_4O_4BrC1$ 256	10.99 [S, 1H, NH indole] 10.88 [S, 1H, NH pyrimidine] 6.6-7.6 [m, 9H, 2Ar-H] 0.9 [t, CH_3], 2.25 [S, 3H, CH_3], 3.8 [q, 2H, $0CH_2$]	13.01	12. 11
C_{15}	H Br H Cl	$C_{22}H_{18}N_4O_4BrC1$ 257	10.99 [S, 1H, NH indole] 10.88 [S, 1H, NH pyrimidine] 6.6-7.6 [m, 9H, 2Ar-H] 0.9 [t, CH_3], 2.25 [S, 3H, CH_3], 3.8 [q, 2H, $0CH_2$]	12.09	11.06
C_{16}	Br H Br Cl	$C_{21}H_{17}N_4O_4Br_2C1$ 259	11.00 [S, 1H, NH indole] 10.92 [S, 1H, NH pyrimidine] 6.4-7.1 [m, 5H, 2Ar-H] 0.9 [t, CH_3], 2.25 [S, 3H, CH_3], 4 [q, 2H, $0CH_2$]	10.22	9.14
C_{17}	H H CH_3 C1	$C_{23}H_{20}N_4O_4C1$ 246	11.00 [S, 1H, NH indole] 10.92 [S, 1H, NH pyrimidine] 6.4-7.1 [m, 5H, 2Ar-H] 0.9 [t, CH_3], 2.25 [S, 3H, CH_3], 4 [q, 2H, $0CH_2$]	18.25	17.02
C_{18}	H H Cl Cl	$C_{22}H_{18}N_4O_4C1_2$ 255	11.00 [S, 1H, NH indole] 10.92 [S, 1H, NH pyrimidine] 6.6-7.6 [m, 5H, 2Ar-H] 0.9 [t, CH_3], 2.25 [S, 3H, CH_3], 4 [q, 2H, $0CH_2$]	16.45	15.19
C_{19}	H H H OH	$C_{22}H_{19}N_4O_5$ 258	420, 11.90 [S, 1H, NH indole] 11.85 [S, 1H, NH pyrimidine] 6.4-7.4 [m, 7H, 2Ar-H] 0.9 [t, CH_3], 2.3 [S, 3H, CH_3], 4 [q, 2H, $0CH_2$]	27.83	26.01
C_{20}	CH_3 H H OH	$C_{23}H_{21}N_4O_5$ 259	11.88 [S, 1H, NH indole] 11.75 [S, 1H, NH pyrimidine] 6.2-7.4 [m, 6H, 2Ar-H] 1.1 [t, , CH_3], 2.6 [S, 3H, CH_3], 3.8 [q, 2H, $0CH_2$]	25.03	23.74
C_{21}	F H H OH	$C_{22}H_{18}N_4O_5F$ 261	11.92 [S, 1H, NH indole] 11.80 [S, 1H, NH pyrimidine] 6.6-7.6 [m, 6H, 2Ar-H] 0.9 [t, CH_3], 2.25 [S, 3H, CH_3], 4 [q, 2H, $0CH_2$]	23.11	21.09
C_{22}	Cl H H OH	$C_{22}H_{18}N_4O_5C1$ 263	11.92 [S, 1H, NH indole] 11.80 [S, 1H, NH pyrimidine] 6.6-7.6 [m, 6H, 2Ar-H] 0.9 [t, CH_3], 2.25 [S, 3H, CH_3], 4 [q, 2H, $0CH_2$]	21.22	20.67
C_{23}	Br H H OH	$C_{22}H_{18}N_4O_5Br$ 266	11.92 [S, 1H, NH indole] 11.80 [S, 1H, NH pyrimidine] 6.6-7.6 [m, 6H, 2Ar-H] 0.9 [t, CH_3], 2.25 [S, 3H, CH_3], 4 [q, 2H, $0CH_2$]	18.92	17.23
C_{24}	H Br H OH	$C_{22}H_{18}N_4O_5Br$ 267	11.92 [S, 1H, NH indole] 11.80 [S, 1H, NH pyrimidine] 6.6-7.6 [m, 6H, 2Ar-H] 0.9 [t, CH_3], 2.25 [S, 3H, CH_3], 4 [q, 2H, $0CH_2$]	19.53	18.09

C_{25}	Br H Br OH	$C_{22}H_{17}N_4O_5Br_2$ 270	11.80 [S, 1H, NH indole] 11.00 [S, 1H, NH pyrimidine] 6.6-7.6 [m, 5H, 2Ar-H] 1.0 [t, CH_3], 2.20 [S, 3H, CH_3], 3.9 [q, 2H, $0CH_2$]	17.11	16.04
C_{26}	H H CH_3 OH	$C_{23}H_{21}N_4O_5$ 258	11.88 [S, 1H, NH indole] 11.75 [S, 1H, NH pyrimidine] 6.2-7.4 [m, 6H, 2Ar-H] 0.9 [t, CH_3], 2.6 [S, 3H, CH_3], 3.8 [q, 2H, $0CH_2$], 3.8 [S, 3H, $0CH_3$]	26.00	24.80
C_{27}	H H Cl OH	$C_{23}H_{22}N_4O_5$ 263	11.88 [S, 1H, NH indole] 11.75 [S, 1H, NH pyrimidine] 6.2-7.4 [m, 6H, 2Ar-H] 0.9 [t, CH_3], 2.6 [HS, 3H, CH_3], 3.8 [q, 2H, $0CH_2$]	22.50	20.09
C_{28}	H H H OCH_3	$C_{23}H_{22}N_4O_5$ 245	43, 11.99 [S, 1H, NH indole] 12.0 [S, 1H, NH pyrimidine] 6.5-7.6 [m, 7H, 2Ar-H] 0.8 [t, CH_3], 2.6 [S, 3H, CH_3], 3.8 [q, 2H, $0CH_2$], 3.8 [S, 3H, CH_3]	28.99	26.75
C_{29}	CH_3 H H OCH_3	$C_{24}H_{23}N_4O_5$ 246	11.90 [S, 1H, NH indole] 11.75 [S, 1H, NH pyrimidine] 6.6-7.6 [m, 7H, 2Ar-H] 0.9 [t, CH_3, 2.5 [S, 3H, CH_3], 4 [q, 2H, $0CH_2$], 6.4 [S, 3H, CH_3], 3.8 [S, 3H, $0CH_3$]	25.53	23.01
C_{30}	F H H OCH_3	$C_{23}H_{21}N_4O_5F$ 248	12.70 [S, 1H, NH indole] 12.0 [S, 1H, NH pyrimidine] 6.2-7.6 [m, 7H, 2Ar-H] 0.9 [t, CH_3], 2.5 [S, 3H, CH_3], 4 [q, 2H, $0CH_2$], 3.8 [S, 3H, OCH_3-Ar]	24.02	21.53
C_{31}	Cl H H OCH_3	$C_{23}H_{21}N_4O_5C1$ 250	12.70 [S, 1H, NH indole] 12.5 [S, 1H, NH pyrimidine] 6.6-7.6 [m, 7, 2Ar-H] 0.9 [t, CH_3], 2.5 [S, 3H, CH_3], 4 [q, 2H, $0CH_2$], 3.8 [S, 3H, $0CH_3$]	20.12	18.88
C_{32}	Br H H OCH_3	$C_{23}H_{21}N_4O_5Br$ 252	12.70 [S, 1H, NH indole] 12.20 [S, 1H, NH pyrimidine] 6.6-7.6 [m, 7H, 2Ar-H] 0.9 [t, CH_3], 2.5 [S, 3H, CH_3], 4 [q, 2H,	19.01	17.89
C_{33}	H Br H OCH_3	$C_{23}H_{21}N_4O_5Br$ 251	12.70 [S, 1H, NH indole] 11.75 [S, 1H, NH pyrimidine] 6.6-7.6 [m, 7H, 2Ar-H] 0.9 [t, CH_3], 2.25 [S, 3H, CH_3], 4 [q, 2H, $0CH_2$]	19.99	18.24
C_{34}	Br H Br OCH_3	$C_{23}H_{20}N_4O_5Br_2$ 254	12.70 [S, 1H, NH indole] 11.75 [S, 1H, NH pyrimidine] 6.6-7.6 [m, 7H, 2Ar-H] 0.9 [t, CH_3], 2.25 [S, 3H, CH_3], 4 [q, 2H, $0CH_2$]	17.58	16.55
C_{35}	H H CH_3 OCH_3	$C_{24}H_{23}N_4O_5$ 246	12.70 [S, 1H, NH indole] 11.75 [S, 1H, NH pyrimidine] 6.6-7.6 [m, 7H, 2Ar-H] 0.9 [t, CH_3], 2.25 [S, 3H, CH_3], 4 [q, 2H, $0CH_2$]	26.80	25.01
C_{36}	H H Cl OCH_3	$C_{23}H_{21}N_4O_5C1$ 251	12.70 [S, 1H, NH indole] 11.75 [S, 1H, NH pyrimidine] 6.6-7.6 [m, 7H, 2Ar-H] 0.9 [t, CH_3], 2.25 [S, 3H, CH_3], 4 [q, 2H, $0CH_2$]	22.15	21.34
			Ascorbic acid	6.02	5.80

evaluated from the difference in peak area decrease of the DPPH radical detected at 517 nm between a blank and test compounds.

Compounds C_1 to C_{36}, consisting of series, X-3[(4-phenyl-5-carboethoxy-6-methyl-3,4-dihydropyrimidin[1*H*]-2-one)indolin-2-ones], Y-3[(4-chlorophenyl-5-carboethoxy-6-methyl-3,4-dihydropyrimidin[1*H*]-2-one)indolin-2-ones], Z-3[(4-hydroxy-phenyl-5-carboethoxy-6-methyl-3,4-dihydropyrimidin[1*H*]-2-one)indolin-2-ones]X1-3[(4-methoxyphenyl-5-carboethoxy-6-methyl-3,4-dihydropyrimidin [1*H*]-2-one)indolin-2-ones showed antioxidant activity by DPPH method by UV spectrophotometer and reversed phase HPLC analysis. The activity represented by IC_{50} values in micro moles (µM). Among all the coumponds series of Y[having 4-chlorobenzaldehyde substituent at 5-position of pyrimidine ring] have promising highest antioxidant activity [$C_{16} > C_{15} > C_{14} > C_{15}$ and C_{12}] followed by z,x_1 and x series. Among isatins, 5,7-disubstituted halogens are more active than mono subsituted halogens against antioxidant activity followed by Br, C1, F. All the results are depicted in Table-1. HPLC method is more sensitive for the above compounds, 2 to 5 % variation found in comparison to UV spectrophotometer.

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