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Antibacterial and Antifungal Investigation of the new Coumarin Derivatives

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ABSTRACT
The 7-cyano-6methyl-3phenonecoumarin was synthesized by reaction of 4-cyano-2-hydroxy-5-methyl benzaldehde with etyl benzoyl acetate,
The new compounds of coumarin dervatives were characterized by ^{1} H-NMR , mass spectroscopy , infrared and elemental analysis. The new compounds exhibited antibacterial and antifungal activites the 6-chloro-3thoxycarbonyl7,8dimethoxy-coumarine was synthesized by reaction 5-bromo-2hydroxy-3,4dimethoxy benzaldehyde with diethlmalonate..
The structures of the prepared compounds 3a, 3b were characterized by IR,^{1}H-NMR, mass spectroscopy and CHN analysis. The new products exhibited antibacterial and antifungal activities.
Keywords: coumarin, elemental analysis and biological activity

I. INTRODUCTION

We have already reported several coumarin derivatives which have significant inflammatory and anti- Oxidant activities [1-3] the coumarin ring has been shown to possess unique anti oedema and anti-inflammatory activities. Thus, cumarin derivatives could be particularly effective in the treatment of all high protein oedemas [4-6]

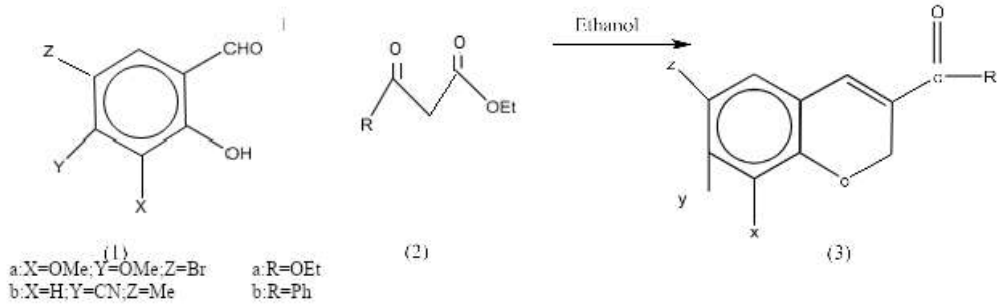
Coumarin derivatives are important chemicals in the perfume, cosmetic, agricultural industries [1]. Inflammatory diseases are becoming common in aginbiociety throughout the world. Recent studies indicate that the mediators and cellular effectors of inflammation are important constituents of the local environment of tumors [2]. The incorporation group as of used component into parent coumarin alters the property of parent coumarin and converts it into a more useful produce [3].

Experimental:
Instrumentation

Melting points were measured on Gallenkamp electronic melting points apparatus, the IR spectra were recorded on a perkin Elmer 317 Grating IR spectrophotometer, using KBr. The ^{1}H-NMR spectra were recorded on a Varian MERCURY 300MHz spectrometer using TMS as internal standed in deuterated dimethyl sulphoxide, the elemental analysis was performed on a perkin-Elmer 2400. The mass spectra were recorded on shimadzu GCMS-Q-P-1000EX mass spectrometer at 70ev.

Synthesis of 6-chloro – 3ethoxycarbonyl 7,8 dimethoxy- coumarin(3a):

Amexture of 5-bromo-2-hyroxy -3,4dimethoxy benzaldehyd (1a,2.17gm,0.01mole) and diethylmalonate (2a,1.60gm, 0.01mole) in round bottom flask (205m) in Absolut ethanol (150m) and 2ml of piperidine was added. The mixture was heated to reflux for 2 hours and keep overnight. The solid products was separated by filtration. The solid was recrystallized from ethanol



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Synthesis of 7 cyano-6methyl-3-phenonecoumarin (3b)

In a round bottom glass (pyrix) flask (500ml) dissolve (1b,16.1gm, 0.1mole) of 4 cyano-2-hydroxy- 5- methyl benzaldehyde in 200ml ethanol then added (2b,19.2gm, 0.1mole) of ethyl benzoyl acetate, stirr the mixture at room temperature for 1 hr. then few drop of piperidine about (2ml) . The mixture was heated to reflux for 2hrs and keep overnight. The solid was separated by filtration .the solid was recrystallized from ethanol.

II. RESULTS AND DISCUSSION:

Infrared and NMR studies of 6 – chloro– 3 ethoxycarbonyl- 7, 8 dimethoxycoumarin (3a).

The infrared spectrum of the (3a) table 2 exhibited a strong bands at 1688 and 1710 cm^{-1}corres ponding to ע (C=O) (100m) and 2ml of piperidine was added .the mixture was heated to reflux for 2 hrs, the reaction mixture was cooled and the brown residue was separated by filtration . the solid was recrystallized from ethanol.)(lactone), ע(C=0) (ester), respectively. ^{1}H-NMRspectra of compound (3a) showed a singlet signals at 2.71 and 2.83 ppm due to (2OCH3) protons. also, the ^{1}H- NMRspectrum exhibit quartet signal at 4.11 ppm (q,2H,CH2) and triplet signal at 1.31 ppm (t,3H,CH3), 7.30-7.68 ppm

(S,1H,Ar-H) and singlet signals at 6.52 ppm (S,1H,pyran ring). The mass spectrum of (3a) the following peaks of m/z values followed by % relative abundances[M] 357(79.16), 327 (51.22), 278 (38.12), 254 (85.27), 218(24.90), 176(40.03), 130 (60.44), 102 (25.14) 77(100).

Infrared and NMR studies of 7- Cyano – 6methyl- 3- phenonecoumarin (3b) The infrared spectrum of (3b) table (2) displayed absorption bands(v/cm^{-1})at 1651 and 1702 corresponding to ע (C=O) (lactone), ע(C=O) (ketone), respectively. The^{1}H-NMR spectrum of the (3b) in deuterated DMSO-d6 of table (2) showed a singlet signal at 2.56ppm due to (CH3), as well as multiplets in range 7.19-7.59 ppm due to phenyl protons .furthermore, asinglet signal at 6.27ppm due to pyran ring proton. The mass spectrum of compound (3b) showed the molecular ion peak at m/z 289(93.16) the following peaks of values followed by % relative abundances (M+1) 290(77.35), 275(29.03), 250(34.14), 216(67.94), 171(74.55),
146(17.40), 127(69.13), 77(83.49), 65(100nb

Biological activity

measurement of antimicrobial activity using diffusion disc method: A filter paper sterilized disc (diameter 80mm) saturated with measured quantity of the sample is placed on plate containing solid bacterial medium (nutrient agar broth) or fungal medium (dox's medium) which has been heavily seeded with the spore suspension of the tested organisms . After incubation the clear zone of inhibitory surrounding the sample is taken as measure of inhibitory power of the sample [32-35].

The experiments were performed using test bacterial organisms belonging to the gram positive and gram negative groups namely staphylococcus aureus and Escherichia coli respectively, as well as aspergillusflavus and candida albicans as tested fungi. The compounds under investigation were dissolved in DMSO as an inactive solvent towards all microorganisms .The concentration of DMSO solutions were 0.2mg/ml. all the tested compunds showed antimicrobial activity and these activities were compared to standard amikacin, the results of antimicrobial studies are given in table 3.

Table 1: physical characterization of coumarin derivatives.

Compound No.	MP.C° Color	Solvent yield %	MF (M.wt)	Elemented analysis calcd/found		
				C%	H%	N%
3a	218-220	Ethanol	C14H13O6Br	53.75	4.19	/
	Brown	76	357.0177	53.01	3.42	/
3b	207-209	Ethanol	C18H11NO3	74.73	3.83	4.84
	Brown	84	289.2889	74.16	3.22	3.99

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Table 2: Spectroscopic data of coumarin derivatives

Compound no.	IR(KBr) ע(cm^{-1})	^{1}H-NMR S(ppm)
3a	(enotcal) 8861 (O=C) ע (retse) 0171 (O=C) ע 8061(C=C) ע	2,71,2,83,(S,6H,2OCH3) 4,11(q,2H,CH2) 1.31(t,3H,CH3) 7.30(S,1H,Ar-H) 6.52(S,H,pyran ring)
3b	0122 (N=C) ע (enotek) 2071(O=C) ע 3951(C=C) ע (enotcal) 1561(O=C) ע	2.56(S,3H, CH3) 7.19(m,2H, Ar-H) 6.27(S,1H, pyran ring)

Table 3: The inhibition zones (mm) of some coumarin derivatives against tested organisms

Sample / standard	Inhibition zone (mm/mg sample)			
	Escherichia coli (G-)	Staphylococcus Aureus (G +)	Aspergillus Flavus (fungus)	Candida albicans (fungus)
3a	21	32	28	23
3b	13	30	24	20

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