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Review article

Coumarins: The Antimicrobial agents

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ABSTRACT
Emergence of resistance by bacterial and fungal stains towards existing antimicrobial agents is one of the major problem as well as motivation to synthesize a new class of antimicrobial agents possessing potent activity compared to commonly used therapy. Coumarin is the heterocyclic compound formed from benzene and pyrone ring containing oxygen and its derivatives are of wide awareness because of their diverse biological activity and clinical applications, they are remarkably effective compounds both with respect to their inhibitory activity and their favourable selectivity ratio. Coumarins are regarded as a promising class of bioactive heterocyclic compounds that exhibit a range of biological activities like anti-microbial, anti-viral, anti-diabetic, anti-cancer activity, anti-oxidant, anti-parasitic, anti-helmintic, anti-proliferative, anti-convulsant, anti-inflammatory and anti-hypertensive activities etc. The information given in this manuscript may be helpful in the further research of better antimicrobial agents having lesser microbial resistance and improved antimicrobial profile.
Key words: Coumarin, Coumarin derivatives, Antimicrobial activity.

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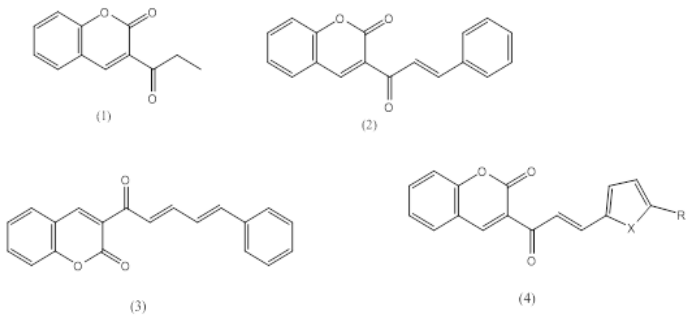
INTRODUCTION

There are a number of reports that natural and synthetic Coumarin derivatives posses antimicrobial activity.[1-14] Novobiocin and Chlorobiocin are established antimicrobials containing a Coumarin (i.e.2H-1-benzopyran-2-ones) skeleton, there are many Coumarin derivatives which have been reported for anticoagulant, anti-inflammatory, anti-HIV, anti-oxidant, anti-allergic, anti-cancer, anti proliferative and antiviral activities.[15-17] It was found that when one biodynamic heterocyclic system was coupled with another heterocyclic system, enhanced biological activity was produced. Drug resistance has become a growing problem in the treatment of infectious diseases caused by bacteria and fungi.[18] The serious medical problem of bacterial and fungal resistance and the rapid rate at which it develops has led to increasing levels of resistance to classical antibiotics,[19,20] and the discovery and development of effective antibacterial and antifungal drugs with novel mechanisms of action have thus become urgent tasks for infectious disease research programs.[21] Coumarins present a variety of bioactivities, including anticoagulant, estrogenic, dermal photosensitizing, antimicrobial, vasodilator, molluscicidal, anti-helmintic, sedative and hypnotic, analgesic and hypothermic actions.[22] Furthermore, the pharmacological properties as well as therapeutic applications of coumarins depend upon the pattern of substitution and recently they are reported to possess many pharmacological activities such as antimicrobial activity. In continuation of previous studies[23-32] on coumarins, herein we are reporting a review for such recent derivatives of coumarins with antioxidant activities.

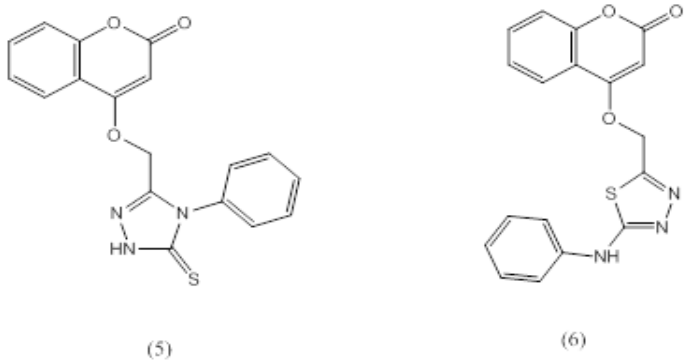


ANTIMICROBAL ACTIVITY

Olayinka O. Ajani *et al.* reported synthesis and biological activities of some substituted coumarins All the compounds(1,2,3,4) showed good activity against *Staphylococcus aureus* and *Escherichia coli* and, *Bacillus subtilis.*[33]

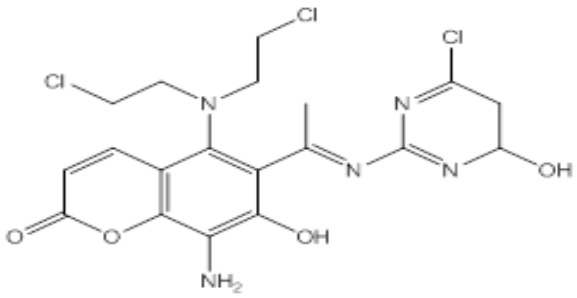
Al-Amiery *et al.* have synthesized 4-[(5-mercapto-4-phenyl-4H-1,2,4-triazol-3-yl)-methoxy]-2H- chromen-2-one as coumarin derivatives and their antifungal activity was determined based on the growth inhibition rates of the mycelia of strains of *Aspergillus niger* and *Candida albicans* in Potato Dextrose Broth medium (PDB) against concentrations ranging from 10 to 100μgml^{-1}. Two compounds (5,6) showed good activity as antifungals against fluconazole standard drug.[34]

Behrami *et al.* synthesized 8-amino-4,7-dihydroxy-chromen-2-one coumarin derivatives. The antibacterial activities of all the compounds and



standard streptomycin and cefalexine at concentractions of 2 mgml^{-1}, 3 mgml^{-1} and 5mgml^{-1} were studied against *Staphylococcus aureus, Bacillus subtilis* and *Escherichia coli*. One compound (7) was more active than cefalexine and lesser active than streptomycin and it was most active among synthesized compounds.[35]

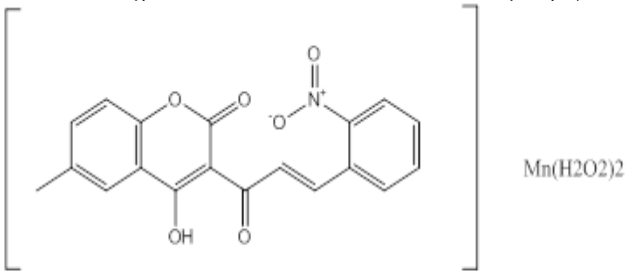
Vyas *et al.* synthesized some novel 3-[{(3-(2'-Nitrophenyl)}-prop-2-enoyl]-4-hydroxy-6-methyl- 2H-chromene-2-ones (8) and their *in-vitro* antimicrobial activity screened against four strains of bacteria such as *Staphylococcus aureus, Bacillus megaterium, Escherichia coli*, and *Proteus vulgaris* and one fungi *Aspergillus niger*. Zone of inhibition of highly active compound was 25 mm as antibacterial agent against *Escherichia coli* compared with standards ampicillin (16 mm), amoxicillin (17 mm),



(7)

ciprofloxacinin (26 mm), erythromycin (22 mm) and was 23 mm as antifungal agent against *Aspergillus niger* compared with standard drug griseofulvin (21 mm).[36]

Behrami *et al* synthesized some novel coumarin derivatives, antibacterial activity of synthesized compounds and standard drugs (streptomycin and cefalexine) at concentrations of 2 $mgml^{-1}$, 3 $mgml^{-1}$ and 5 $mgml^{-1}$ were evaluated against three strains of bacterial culture, *Staphylococcus*



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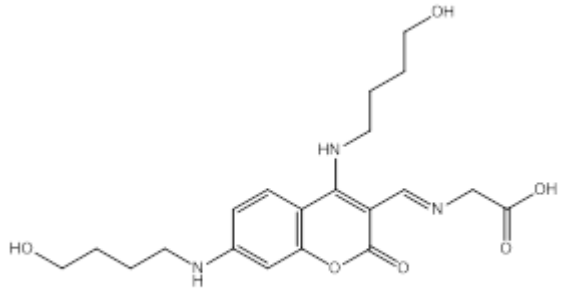
aureus, *Escherichia coli* and *Bacillus cereus*. One compound (9) showed a significant antibacterial effect against *S. aureus*, *Escherichia coli* and *Bacillus cereus*.[37]



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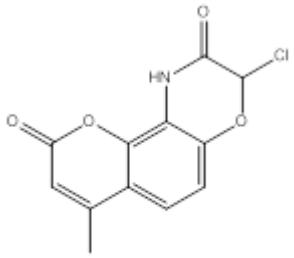
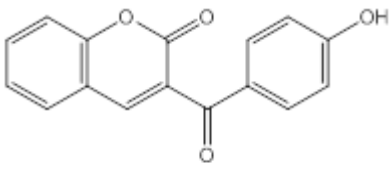
Bonsignore *et al*. synthesized a novel series of comarin 7-substituted cephalosporins and sulfones. The synthesized compounds were tested against *Staphylococcus aureus* (ATCC 25923), *Escherichia coli* (ATCC 25922) and *Pseudomonas aeruginosa* (ATCC 27853) with varying concentrations of the associated antibiotic cefotaxime (0.125-256 μgml^{-1}) Cephalosporins showed a potential activity against Gram positive microorganisms and sulfones showed no significant activity. An association of sulfone with ampicillin was observed to inhibit Gram positive microorganisms with a lower MIC value than for ampicillin alone.[38]

Novel coumarin derivatives were synthesised by Sahoo *et al*. and antibacterial activity was tested against Gram positive bacteria i.e. *Staphylococcus aureus* and Gram negative bacteria i.e. *Escherichia coli*. DMSO was used as a control. One compound (10) possessed maximum antibacterial activity as compared to standard drug amoxicillin which may be due to presence of chlorine on aromatic ring of coumarins. Other compounds also showed mild to moderate activity at 0.1ml concentration level on both organisms.[39]



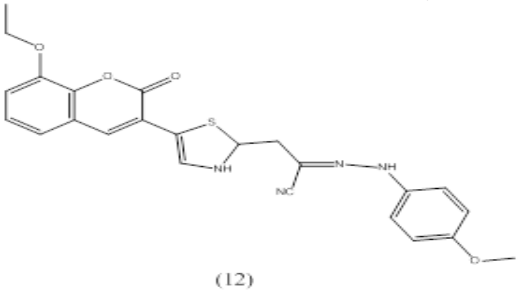
(10)

Purohit *et al* reported synthesis and biological activities of some substituted 3-(4- hydroxybenzoyl)-1H-isochromen-1-one ,2-benzopyran-1H-2-one,1H-2-oxo-benzopyran-3- carboxylicacids and 2-benzofuran-1H-one. All the compounds showed good activity against *Staphylococcus aureus* and *Escherichia coli*.[40]



(11)

Mohamed *et al*. derivatised some novel 8-ethoxycoumarin and screened for their *in-vitro* antimicrobial activities against two Gram negative *Bordetella bronchiseptica* (ATCC 4617) and *Escherichia coli* (ATCC 14169) and four Gram positive *Bacillus pumilus* (ATCC 14884), *Bacillus subtilis* (ATCC 6633), *Staphylococcus aureus* (ATCC 29737) and *Staphylococcus epidermidis* (ATCC 12228) *pathogenic bacteria* and two fungi *Candida albicans* (ATCC 10231) and *Saccharomyces cervesia* (ATCC 9080). One compound (12) resulted in wide spectrum antimicrobial activity against all tested bacteria and fungi compared to ampicillin ($25\mu gml^{-1}$) and *mycostatin* ($25\mu gml^{-1}$) by replacing the hydrogen atom attached to the coumarin nucleus at C-3 with a side chain, while the other compounds with other side chains showed moderate to weak activity.[41]

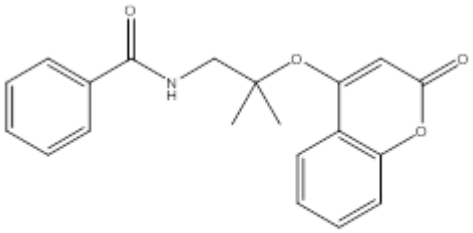


(12)

Mulwad VV *et al*. synthesized some heterocycles by incorporating isoxazoles, pyromidines and 1,5- benzothiazeoine in a parent 4-hydroxycoumarin molecule which enhanced the biological properties of these molecules. These compounds were tested for *in vitro* antibacterial activity.[42]

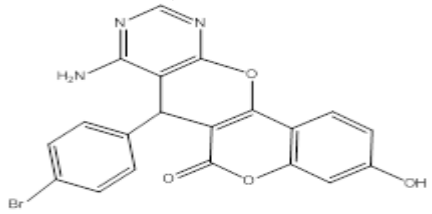
Gupta AS *et al*. synthesized 3- amino-(N-aryl substituted)-6-bromo-2H-1-benzopyran-2- ones and 6-bromo-3-phenoxy substituted-2H-1-benzopyran-2-ones. All the title compounds were screened for *in-vitro* antitubercular activity against highly virulent H37Rv strains of mycobacterium tuberculosis as compared to streptomycin and INH.[43,44] Lin

et al. synthesized acyl coumarins, 4-hydroxy, and 7-hydroxycoumarins and coumaric amide dimers and were tested against stains of *Bacillus subtilis* (BCRC 10029), *Staphylococcus aureus* (BCRC 11863), *Escherichia coli* (BCRC 11758), and *Pseudomonas aeruginosa* (BCRC 11733) and Penicillin G potassium salt (CAS 113-98-4, USP grade) was used as a reference drug. One compound (13) was the most potent compound out of the tested compounds against Bacillus subtilis with MIC value of 8 μgml^{-1}.[45]



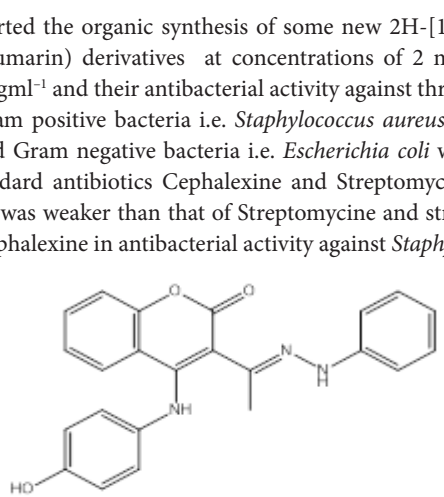
(13)

Kusanur RA *et al*. developed the new 1,3-dipolar cycloadducts of 3-azidoacetylcoumarins with dimethyl acetylene dicarboxylate (DMAD). All the newly synthesized compounds and their adducts were screened for antimicrobial activity and good results were obtained.[46] Pyrimidino[5',4'-6,5]-,pyridino[3',2'-6,5] and pyrrolo[3',2'-5,6]4H-pyrano-[3,2-c][1] benzopyran- 6-one derivatives were prepared and screened by Al-Haiza *et al.* for their activity against Gram positive bacteria, *Staphylococcus aureus*, *Bacillus subtilis*, *Bacillus cereus,* Gram negative bacteria, *Pseudomonas aurignosa*, *Echerichia coli*, *Enterobacter aerogenes* as well as fungi *Aspergillus niger*, *Penicillium italicum*, *Fusarium oxysporum*. Standard drugs amoxicillin for bacteria and mycostatin for fungi were used at a concentration of 1000ppm for comparisons. One compound (14) exhibited excellent antibacterial activity towards *Enterobacter aerogenes.*[47]



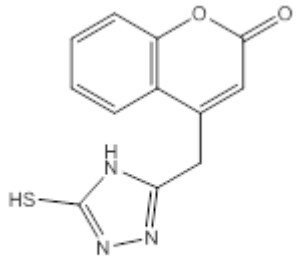
(14)

Vaso *et al*. reported the organic synthesis of some new 2H-[1]-benzopyran-2-one(coumarin) derivatives at concentrations of 2 $mgml^{-1}$, 3 $mgml^{-1}$ and 5 $mgml^{-1}$ and their antibacterial activity against three bacterial cultures Gram positive bacteria i.e. *Staphylococcus aureus* and *Bacillus aureus* and Gram negative bacteria i.e. *Escherichia coli* was compared with standard antibiotics Cephalexine and Streptomycine. One compound (15) was weaker than that of Streptomycine and stronger as compared to Cephalexine in antibacterial activity against *Staphylococcus aureus.*[48]



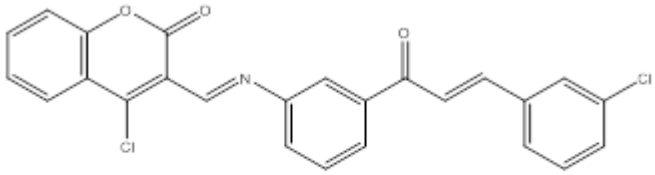
(15)

Some derivatives of (7-hydroxy-2-oxo-2H-chromen-4-yl)-acetic acid hydrazide (16) were prepared by Cacic *et al*. and were found to possess high antimicrobial activity against *Staphyloccocus pneumoniae* and were slightly less active against *Pseudomonas aeruginosa*, *Bacillus subtilis*, *Bacillus cereus* and *Salmonela panama* as compared to standard drug.[49]



(16)

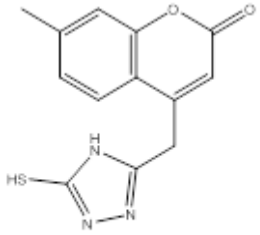
A series of the Schiff's bases, 3-(4-(4-(substituted phenyl)prop-1-ene-3-one)phenylimino) methyl)-4-chloro-2H-chromen-2-ones were synthesized by Kudale *et al*. and these compounds were investigated *in-vitro* against gram positive bacteria, *Staphylococcus aureus* (ATCC 9144), *Bacillus subtilis* (ATCC 6633) and *Staphylococcus epidermis* (ATCC 12228) and gram negative bacteria, *Escherichia coli* (ATCC 25922), *Salmonella typhi* and *Psuedomonas aeruginosa* (ATCC 9027) and the antifungal activity was evaluated against *Aspergillus niger* (ATCC 10594) and *Clostridium albicans* (ATCC 10231) using amoxicillin and fluconazole as standard drugs for antibacterial and antifungal activities respectively. One compound (17) was found to be most active with an MIC of 20μgml^{-1}against all the tested organisms.[50]



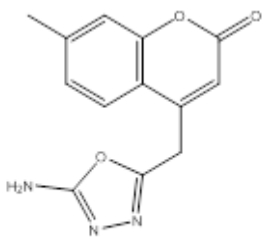
(17)

Hamdi *et al* synthesized bis[N-(4-oxocoumarinylmethylene)]-1,4-diamines and the antibacterial activity tests were carried out using *Staphylococcus aureus* ATCC 25923 at a concentration of 106CFCml–1 on the surface of a Mueller-Hint on gelose plate. One compound exhibited the strongest antibacterial activity.[51] Mashelkar *et al*. synthesized some novel 4-substituted coumarins and subjected them to *in-vitro* screening against Gram positive *Staphylococcus aureus* and Gram negative *Salmonella typhi*. Ampicillin and trimethoprim were used as standard drugs. Two compounds (18a-18b) showed significant antibacterial activity at concentration levels of 10 to 200μgml^{-1}against *Staphylococcus aureus* and *Salmonella typhi.*[52]

Dekic *et al*. synthesized 4-arylamino-3-nitrocoumarins and were evalu-

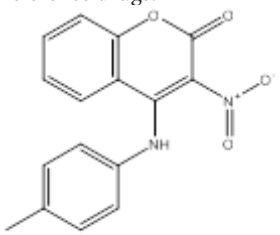


(18a)



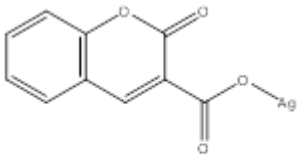
(18b)

ated for their in-vitro antibacterial and antifungal activities against pathogenic strains *Staphylococcus aureus* ATCC 6538, *Bacillus cereus*, *Bacillus subtilis* ATCC 6633, *Escherichia coli* ATCC 8739, *Escherichia coli*, *Klebsiella pneumoniae* ATCC 10031, *Salmonella enterica* ATCC 13076 and yeast *Candida albicans* ATCC 10231 and *Aspergillus niger* ATCC 16404. One compound (19) was found greatest anticandidal as compared with other compounds of the series. Tetracycline and Nystatine were used as the reference drugs.[53]



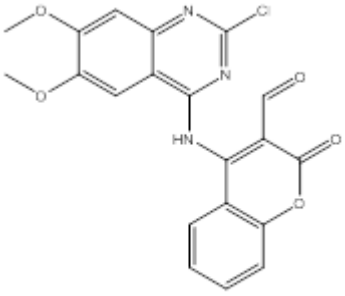
(19)

A series of new coumarin derived carboxylate ligands and their silver(I) complexes (20) were synthesized, characterized and screened by Creaven *et al.* for their *in-vitro* antibacterial activity against a range of Gram positive stains and Gram negative as well as for their antifungal activity. While none of the ligands showed any antimicrobial activity, a number of the Ag(I) complexes exhibited potent activity. In particular, Ag(I) complexes of hydroxy-substituted coumarin carboxylates demonstrated potent activity.[54]



(20)

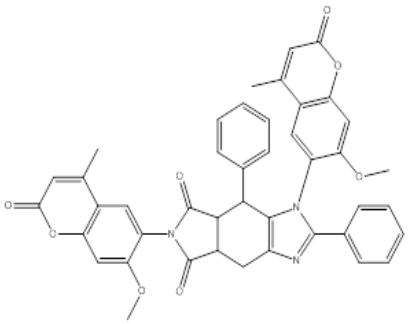
Govori *et al.* synthesized 4-Heteroaryl-coumarin-3-carbaldehydes and antimicrobial properties of these new coumarins were investigated against *Staphylococcus aureus*, *Escherichia coli*, *Hafnia alvei*, *Pseudomonas aeruginosa* and *Enterobacter cloacae*. The Agar disc diffusion technique measured the diameters of the inhibition zone around discs which were previously wetted with N,N-DMF solution of compounds at concentrations of 1,3 and 5mgml^{-1}. One compound (21) was more active against *Staphylococcus aureus*, *Escherichia coli* and *Enterobacter cloaco* and not active as antimicrobial agent against *Hafnia alvei* and *Pseudomonas aeruginosa*.[55]



(21)

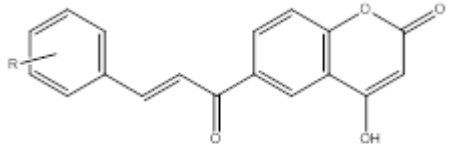
Mulwad VV *et al.* synthesized 4-[1-(2H-[1]-4-hydroxy-2-oxo-benzopyran-3-yl)methylidene]-2- phenyl-4H-oxazol-5-ones and [1,2,4]triazine-6-one and its derivatives. All the compounds were screened for antimicrobial activity and found to exhibit significant activity.[56]

A novel series of 5H,7H-N-(coumarin-6-yl)-2,8-diphenyl-5,7-dioxo-6-(7-methoxy-4-methyl coumarin-6-yl)-4,5,6,7-tetrahydrobenzimidazo[5,6-c]pyrrole derivatives (22) was synthesized and screened by Choudhari *et al.* for their antibacterial activity against *Staphylococcus aureus* and *Salmonella typhi* and antifungal activity against *Aspergillus niger* and *Clostridium albicans*. Ciprofloxacin and miconazole were used as the antibacterial and antifungal standards respectively. All compounds showed antimicrobial activity having MIC values ranging from 50μgml^{-1} to 200μgml^{-1}.[57]



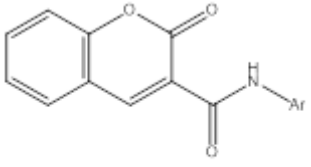
(22)

Zavrsnik D *et al.* prepared a series of new 3-cynnamoyl-4-hydroxycoumarins (23). The microbial activity of the synthesized compounds was tested on species of bacteria *Pseudomonas aeruginosa*, *Echerichia coli*, *Salmonella typhimurium*, *Bordatella bronchiseptica, Bacillus subtilis* and *Staphyloccocus aureus*. The compounds having halogens showed the best microbial activity. Compounds having 4-Br and 4-Cl were found to be the most effective against Bacillus subtilis. Compound having 4-Cl was found to be the most effective against *Staphyloccocus aureus*.[58]



(23)

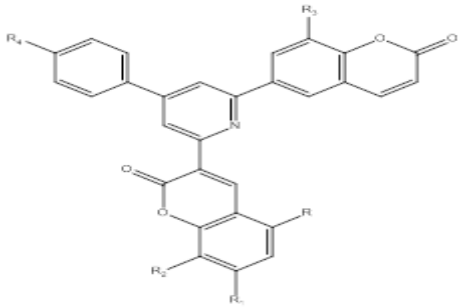
Chimenti F *et al.* prepared N-substituted-2-oxo-2H-1-benzopyran-3-carboxamides (coumarin-3- carboxamides) (24) as new anti-Helicobacter pylori agents and evaluated them for antibacterial activity. All the synthesized compounds showed little or no activity against different species of Gram positive and Gram negative bacteria and against various strains of pathogenic fungi. Among the prepared compounds having 4-acyl phenyl group showed the best activity against Helicobacter pylori metronidazole resistant strains in the 0.25^{-1}μgml^{-1} range, indicating that the presence of an acyl function is an important feature for activity.[59]



(24)

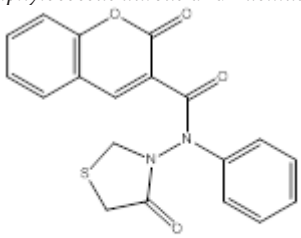
Patel AK *et al.* synthesized some 4-aryl-2,6-di(coumarin-3- yl)pyridines (25) and were tested for antimicrobial activity. None of the compounds

showed antifungal activity against *Aspergillus niger*. The results revealed that the incorporation of the substituents like -CH_3 or -OCH_3 either in the coumarin nucleus or in a phenyl ring did not affect the antibacterial activity much more and all the compounds had almost same activity. Activity of some compounds indicated that the presence of an additional fused benzene ring between the C-5' and C-6' positions inhibited the anti-bacterial activity towards *Escherichia coli*.[60]



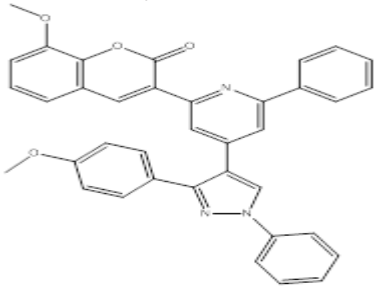
(25)

Some coumarin derivatives containing thiazolidin-4-one ring were synthesized by Rama Ganesh *et al.* and were screened for their antibacterial activity against Gram positive bacteria *Staphylococcus aureus*, *Bacillus subtilis* and Gram negative bacteria *Klebsiella pneumonia*, and *Escherichia coli* at the concentration of 0.001molml^{-1} compared with standard drug Ciprofloxacin. Zone of inhibition of highly active compound (26) was 20 mm against *Staphylococcus aureus* and *Bacillus subtilis*.[61]



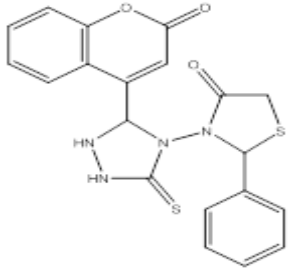
(26)

Brahm Bhatt *et al*. synthesized 4-methyl-3-phenyl-6-[4-(3-aryl-1-phenyl-1H-pyrazol-4-yl)-6-aryl- pyridin-2-yl]coumarin derivatives (27) and were screened for anti-bacterial activity against *Escherichia coli*, *Bacillus subtillis* and anti-fungal activity against Candida albican by agar cup diffusion method. DMF was used as blank, Streptomycin was used as anti-bacterial standard and Clotrimazole as anti-fungal standard drug at concentration of 1000 μgml^{-1}. All the synthesized compounds showed activity against both gram positive and gram negative bacteria but lesser activity compared to standard drug.[62]



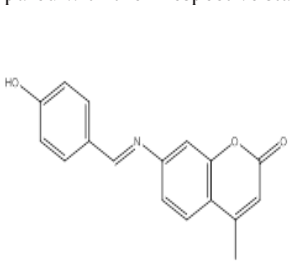
(27)

Bhatt *et al*. synthesized a series of 2-(substitutedphenyl)-3-[3-(2-oxo-2H-coumarin-3-yl)-5- thioxo-1,5-dihydro-4H-1,2,4-triazol-4-yl]-1,3-thiazolidin-4-ones and screened for their antimicrobial activity against Gram positive *Staphylococcus aureus* and Gram negative *Escherichia coli stains* and antifungal activity against *Clostridium albicans*. Ciprofloxacin and ketoconazole were used as the standard antibacterial and antifungal drugs respectively. The test compounds and standards drugs were evaluated at concentration of 100μg/mL. DM F (N,N- dimethylformamide) was used as solvent and control. One compound (28) showed 92%, 80% and 90% growth inhibition against *Staphylococcus aureus*, *Escherichia coli* and *Clostridium albicans* respectively.[63]

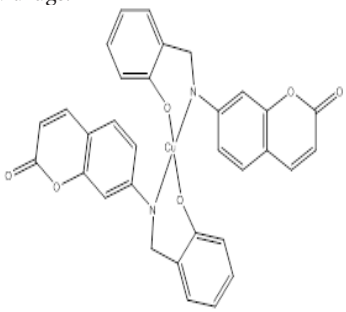


(28)

Creaven *et al*. prepared a series of Schiff bases and Cu(II) complexes (29a-29b). All of the free ligands and their metal complexes were tested for their antifungal activity compared with ketoconazole and amphotericin B. The ligands showed no antimicrobial activity whereas a number of the metal complexes exhibited potent antimicrobial activity when compared with their respective standard drugs.[64]

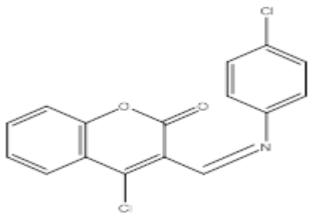


(29a)



(29b)

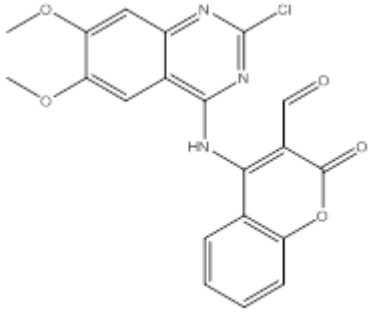
4-chloro-3-((subst it ut ed-phenylimino)methyl)-2H-chromen-2-ones were synthesized by Bairagi *et al*. and tested for antimicrobial activity *in-vitro* against Gram positive *Staphylococcus aureus* (ATCC 29737) and *Bacillus subtilis* (ATCC 2063) and Gram negative bacteria *Escherichia coli* (ATCC 20931) and fungi *Aspergillus niger* (ATCC 16404) and *Candida albicans* (ATCC 10231). One compound (30) was found to be most active against all the tested organisms with an MIC of 15 μgml^{-1}. Amoxicillin was standard for antibacterial activity and fluconazole for antifungal activity.[65]



(30)

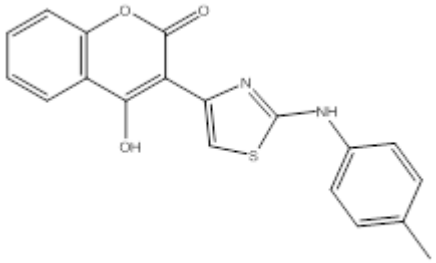
Hafnia alvei, *Pseudomonas aeruginosa* and *Enterobacter cloacae*. The Agar disc diffusion technique measured the diameters of the inhibition zone around discs which were previously wetted with N,N-DMF solu-

tion of compounds at concentrations of 1,3 and 5 $mgml^{-1}$. One compound (31) was more active against *Staphylococcus aureus, Escherichia coli* and *Enterobacter cloaco* and not active as antimicrobial agent against *Hafnia alvei* and *Pseudomonas aeruginosa*.[66]



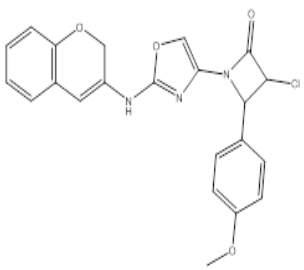
(31)

Novel 4-hydroxy-chromene-2-one derivatives were synthesized by Mladenovic *et al*. and screened for their antibacterial activity against Gram positive bacteria *Staphylococcus aureus*, *Bacillus subtili* and Gram negative bacteria *Klebsiella pneumonia*, *Escherichia coli* and their antifungal activity against *M. mucedo*, *C. albicans*. Streptomycin was used as standard anti- bacterial drug and ketoconazole as standard antifungal drug. One compound (32) had activity equal to that of standard drug ketoconazole (31.25 μgml^{-1}) against M. mucedo.[67]

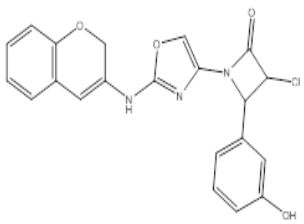


(32)

A novel series of 3-[(2'-Substituted benzylidene amino thiazol-4'-yl) amino]coumarins (33a-33b) was prepared by Singh *et al.* and evaluated for antibacterial activity against various bacteria, *Staphylococcus aureus* 209 P, *E. Coli* ESS2231, *Proteus vulgaris, K. Pneumoniae* were used and antifungal activity was performed against *Candida albicans* ATCC10231 and results were compared with gattifloxacin and ciprofloxacin for antibacterial and fluconazole for antifungal activities respectively and propylene glycol treated group served as control. One compound showed potent antibacterial activity while the other compound exhibited most potent antifungal activity.[68]

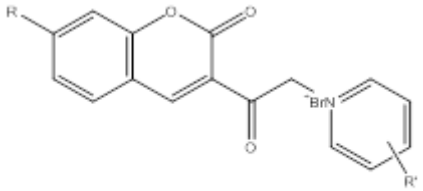


(33a)



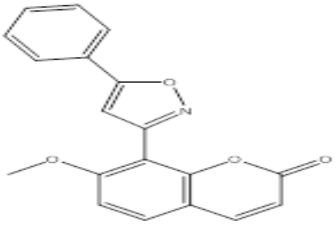
(33b)

Porwal B *et al*. synthesized 3-coumrinoyl pyridinium bromides (34) by reaction of methyl and ethyl esters of nicotinic acid with isonicotinic acid and 3-coumarinoyl quinolinium bromides by reaction of methyl and ethyl esters of nicotinic acid with quinoline. Most of the tested compounds possessed significant antimicrobial activity when compared with that of gentamycin and amoxycillin. The test compounds showing good qualitative antimicrobial property were further screened for their quantitative antimicrobial study by 96-well plate (Two fold dilution technique) using an ELISA Reader. Coumarinoyl pyridinium salts having R = -H & R' = 4-$COOC_2H_5$, R = -Cl & R' = 4-$COOC_2H_5$, R = -H & R' = 3-$COOC_2H_5$ and R = -Cl & R' = 4-$COOCH_3$ were found to be more active than that of other test compounds.[69]



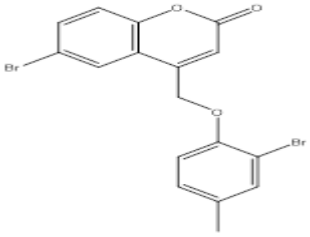
(34)

A new series of 7–methoxy-4-methyl-8-[5-(substituted aryl)isoxazol-3-yl]–2H–benzopyran-2- ones were synthesized by Sandeep *et al*. Antimicrobial activity was carried out against 24 hr old cultures of *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Bacillus subtilis*. The fungi used were *Aspergillus niger*, *Aspergillus flavus* and *Candida albicans*. The compounds were tested at concentrations of 25µg/ml in dimethylformamide against all the organisms. Ciprofloxacin ($25\mu gml^{-1}$) and fluconazole ($25\mu gml^{-1}$) were used as standard drugs for antibacterial and antifungal activities respectively. Among the compounds tested for antibacterial activity, one compound (35) showed highest zone of inhibition against *S. aureus* and *B. subtilis* and minimum inhibition against *E. coli* and *P. aeruginosa*. The remaining compounds exhibited moderate activity.[70]



(35)

Basanagouda *et al*. synthesized 4-aryloxmethylcoumarins (36) and screened for their antibacterial and antifungal activity at different concentrations of 500, 250, 100 and 50 µgml–1 by the disc diffusion method. Antibacterial activity was carried out against two Gram positive bacteria, viz. *Staphylococcus aureus*, and *Streptococcus faecalis* and three Gram negative bacteria, viz. *Escherichia coli*, *Psuedomonus aeruginosa*, *Klebsiella pneumonia*. Antifungal activity was carried out against five fungi, viz. *Aspergillus flavus, Aspergillus fumigatus, Candida albicans, Penicillium notatum* and *Rhizopus*. Ciprofloxacin and Fluconazole were used as standard antibacterial and antifungal drug respectively. The compounds possessing methoxy, chloro, bromo substituents at C-6 position of cou-



(36)

marin showed higher activity.[71]

CONCLUSION

In summary, studies evaluating the antimicrobial activities elicited by coumarinswhich have currently expanded and, though there is plenty of *in vitro* evidence to back up the antimicrobial activities of these compounds, the *in vivo* studies available notably indicate the need to interpret data with caution. In this context, the real antimicrobial effect obtained from oral ingestion of either synthesized or natural compounds and more specifically the suitable dose to achieve this effect for several compounds is still to be proved *in vivo.* Recent studies point towards the rational development of less toxic and more potent compounds which might be clinically utilized in treatment of patients suffering from diseases. However, in spite of tangible advances in drug design and Medicinal Chemistry, there are still few potent pharmacological agents being adopted as antimicrobail in clinical phase. The advances in this field have led to the design and synthesis of new promising prototypes with coumarin. Indeed, these compounds possess several biological activities and their structures allow diverse substitutions and draw much interest considering the possibilities of synthesizing new antimicrobail compounds.

ACKNOWLEDGEMENT

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CONFLICT OF INTEREST

None

ABBREVIATION USED

PDB: Potato Dextrose Broth medium; *E-coli: Escherichia coli*; Coumarin: 2H-[1]-benzo¬pyran-2-one; Ag: Silver; DMF: N,N- dimethylformamide.

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SUMMARY

Coumarin derivatives are known for more than a century. Coumarin derivatives are a plentiful source of potential drugs candidate in relation to their safety and efficacy. This review summarized the antimicrobial activities of some coumarin derivatives.

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