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A REVIEW ON BIOLOGICAL ACTIVITIES OF COUMARIN DERIVATIVES

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ABSTRACT

Coumarins, which are derived from plants, encompass a wide range of structurally diverse natural substances that exhibit various bioactivities. The aim of this paper is to present an introduction to coumarins and their applications as medicinal agents. Coumarin, a heterocyclic compound formed by the fusion of a benzene ring and a pyrone ring containing oxygen, and its derivatives are widely recognized due to their diverse biological activity and clinical applications. These compounds are highly effective in terms of their inhibitory activity and favorable selectivity ratio. Coumarins are considered a promising category of bioactive heterocyclic compounds that demonstrate a multitude of biological activities, such as antimicrobial, antiviral, antidiabetic, anticancer, antioxidant, antiparasitic, anthelmintic, antiproliferative, anticonvulsant, anti-inflammatory, and antihypertensive activities, among others. The information provided in this manuscript could potentially aid in further research on the development of improved antimicrobial agents with reduced microbial resistance and enhanced antimicrobial profile.

KEYWORDS: Coumarin, Coumarin derivatives, Antimicrobial activity.

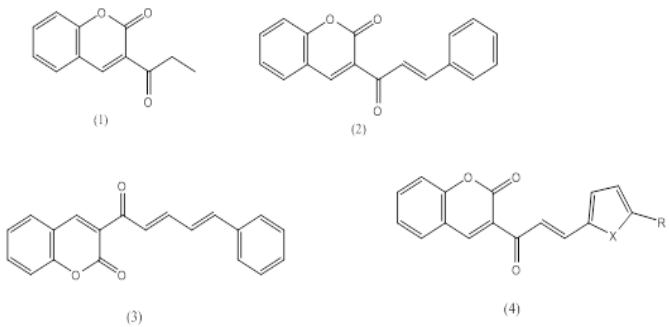
INTRODUCTION

Many reports have demonstrated that compounds of coumarin, both natural and synthetic, possess antibacterial action.[1–14] These compounds, which include Novobiocin and Chlorobiocin, have a coumarin skeleton and have been shown to be effective antibacterial agents. There have also been reports of the diverse activity of a number of additional Coumarin derivatives, such as antiviral, anticoagulant, antioxidant, anti-HIV, anti-allergic, and anti-cancer properties.[15–17] It has been shown that an increase in biological activity occurs when two heterocyclic systems that are biodynamically coupled together. Drug resistance has grown to be a significant concern in the management of bacterial and fungal-caused infectious illnesses. Resistance to conventional antibiotics has increased due to the increasing rate of bacterial and fungal resistance development.[20,19,18] As a result, the creation of potent antibacterial and antifungal medications with unique modes of action is desperately needed, and this area of study has taken center stage in programs that study infectious diseases.[21] A wide variety of biological activities are displayed by coumarins, including

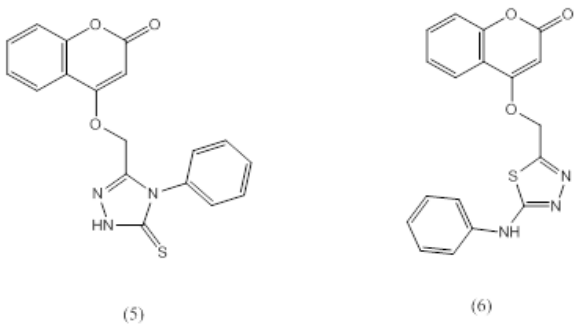
sedative and hypnotic, analgesic, anticoagulant, estrogenic, dermal photosensitizing, antimicrobial, vasodilator, molluscicidal, and hypothermic effects.[22] Moreover, coumarins' pharmacological characteristics and therapeutic uses depend on the pattern of substitution; more recently, it has been discovered that they exhibit a variety of pharmacological actions, including antibacterial activity. Following up on earlier coumarin research projects.[23–32] This study offers an in-depth analysis of the most recent coumarin compounds that exhibit antioxidant properties.

Biological Activity

Olayinka O. Ajani et al. reported the synthesis and analysis of the biological activities of many substituted coumarins in their study. The compounds (1, 2, 3, 4) demonstrated significant effectiveness against Bacillus subtilis, Escherichia coli, and Staphylococcus aureus.[33] Additionally, 4-[(5-mercapto-4-phenyl-4H-1,2,4-triazol-3-yl)-methoxy]-2H-chromen-2-one was produced as a coumarin derivative in a work by Al-Amiery et al. By assessing the inhibition rates of the mycelia of Aspergillus niger and Candida albicans strains in Potato Dextrose Broth medium (PDB) at concentrations ranging from 10 to 100μgml–1, they evaluated the antifungal activity of these compounds. It's interesting to note that two compounds (5,6) showed strong antifungal activity that was on par with the common medication fluconazole.[34]



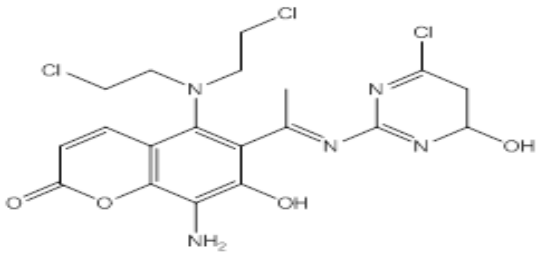
8-amino-4,7-dihydroxy-chromen-2-one is one of the coumarin derivatives that Behrami and associates synthesized. These compounds' antimicrobial qualities were also assessed.



The effects of standard streptomycin and cefalexine against Staphylococcus aureus, Bacillus subtilis, and Escherichia coli were studied at dosages of 2 mg/ml, 3 mg/ml, and 5 mg/ml. One particular chemical, number seven, showed less action than streptomycin but more activity than cefalexine. Out of all the chemicals that were created, this one also showed the highest level of activity.[35]

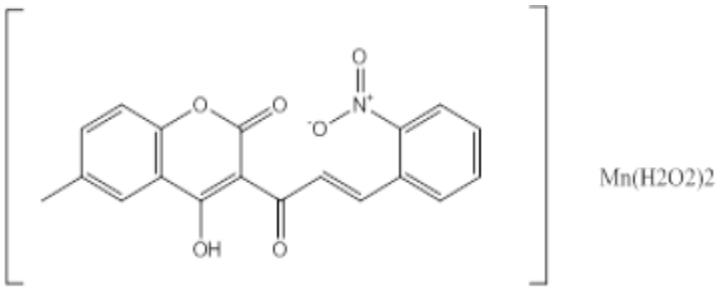
Researchers Vyas et al. synthesized new 3-[{(3-(2'-Nitrophenyl)}2-propenoyl]-4-hydroxy-6-methyl-2H-chromene-2-ones (8) and evaluated their in vitro antibacterial activity against Aspergillus niger and four bacterial strains: Bacillus

megaterium, Proteus vulgaris, Escherichia coli, and Staphylococcus aureus. Comparing the extremely active chemical to the mainstream medications ampicillin (16 mm) and amoxicillin (17 mm), the compound demonstrated a zone of inhibition of 25 mm as an antibacterial agent against Escherichia coli.



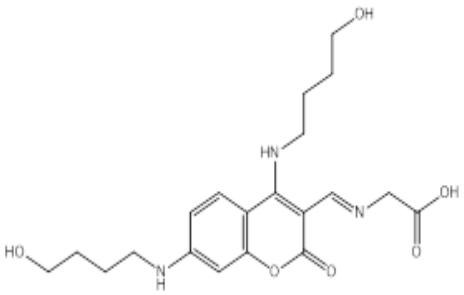
(7)

The zone of inhibition for erythromycin was 22 mm, whereas the zone for ciprofloxacin was 26 mm. When ciprofloxacinin was used against Aspergillus niger, it showed a 23 mm zone of inhibition as opposed to the 21 mm zone of inhibition of griseofulvin, the conventional medication.[36] The synthesis of new coumarin derivatives was the focus of this work by Behrami et al. Three bacterial strains were tested for the antibacterial activity of these produced compounds, as well as common medications like cefalexine and streptomycin: Staphylococcus aureus, Escherichia coli, and Bacillus cereus. At two, three, and five milligrams per milliliter, one



(8)

compound (9) demonstrated a notable antibacterial effect against all three bacterial strains.[37]

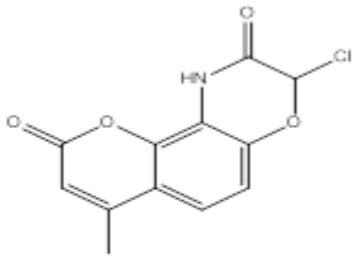


(9)

A novel family of cephalosporins and sulfones containing a comarin substitution at the 7-position was synthesized by Bonsignore et al. Following synthesis, the compounds were tested using different concentrations of the antibiotic cefotaxime (ranging from 0.125 to 256 μg/ml) against Staphylococcus aureus (ATCC 25923), Escherichia coli (ATCC 25922), and Pseudomonas aeruginosa (ATCC 27853). While the sulfones showed no discernible effect, the

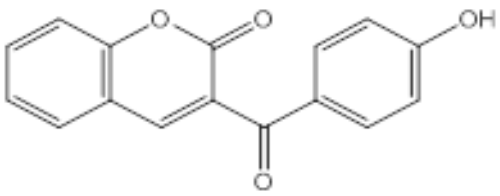
cephalosporins showed potential activity against Gram-positive bacteria. Additionally, a correlation between sulfone and ampicillin was found to inhibit Gram-positive germs, with a minimum inhibitory concentration (MIC) value that was lower than that of ampicillin alone.[38]

Sahoo and colleagues synthesized new coumarin derivatives and assessed their antibacterial efficacy against Escherichia coli and Staphylococcus aureus, two types of bacteria that are Gram-positive and Gram-negative, respectively. In the trials, dimethyl sulfoxide (DMSO) was used as a control. Comparing compound 10 to the common medication amoxicillin, compound 10 had the strongest antibacterial activity of all the compounds examined. It is possible that the presence of chlorine on the aromatic ring of the coumarins is responsible for this increased activity. At a concentration level of 0.1 ml, the other chemicals also showed mild to moderate efficacy against both species.[39]



(10)

A study on the synthesis and biological characteristics of several substituted 3-(4-hydroxybenzoyl)-1H-isochromen-1-one, 2-benzopyran-1H-2-one, 1-H-2-oxo-benzopyran-3-carboxylic acids, and 2-benzofuran-1H-one was presented by Purohit and associates. Purohit et al.[40] reported that the compounds had noteworthy effectiveness in combating Staphylococcus aureus and Escherichia coli.



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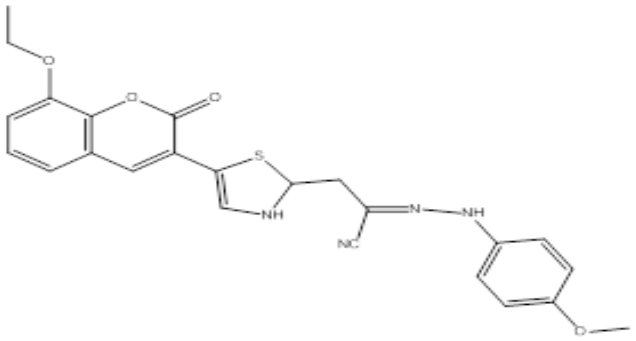
In a research project, Mohamed and associates created novel 8-ethoxycoumarin compounds. The antibacterial properties of these compounds were further investigated in lab settings. The antimicrobial activities were assessed against four different strains of Gram-positive bacteria: Bacillus pumilus (ATCC 14884), Bacillus subtilis (ATCC 6633), Staphylococcus aureus (ATCC 29737), and Staphylococcus epidermidis (ATCC 12228). The two strains of Gram-negative bacteria were Bor-detella bronchiseptica (ATCC 4617) and Escherichia coli (ATCC 14169). Furthermore, the screening procedure included two different species of fungi: Saccharomyces cervesia (ATCC 9080) and Candida albicans (ATCC 10231). A specific chemical (12) exhibited a wide range of antibacterial activity against every tested type of bacteria and fungal. Comparing this chemical to ampicillin (25µg/ml) and mycostatin (25µg/ml), better results were obtained. The substitution of a side chain for a hydrogen atom bonded to the coumarin nucleus at position C-3 was identified as the cause of the increased activity. Conversely, the residual compounds that had distinct

side chains had variable levels of moderate to weak antibacterial activity. Sadly, we were unable to paraphrase the input text's final sentence. As a result, nothing changes.[41]

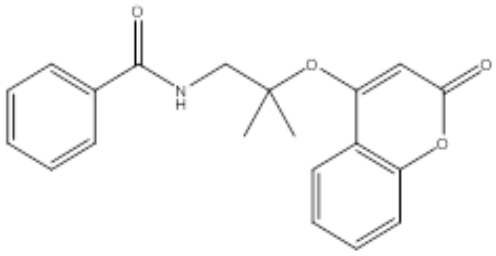


(12)

By adding isoxazoles, pyrimidines, and 1,5-benzothiazeoine to a parent 4-hydroxycoumarin molecule, Mulwad VV et al. synthesized a variety of heterocycles that improved the biological characteristics of the original molecule. Subsequently, the antibacterial activity of these compounds was evaluated in vitro.[42]

3-amino-(N-aryl substituted)-6-bromo-2H-1-benzopyran-2-ones and 6-bromo-3-phenoxy substituted were synthesized by Gupta AS et al.2-H-1-benzopyran-2-ones. After being screened for in-vitro antitubercular efficacy against highly virulent H37Rv strains of mycobacterium tuberculosis, these newly synthesized compounds were compared to streptomycin and INH.[43,44]

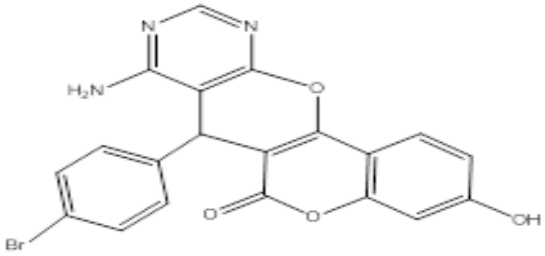
The synthesis of acyl coumarins, 4-hydroxy and 7-hydroxycoumarins, and coumaric amide dimers was carried out by Lin et al. These substances were then tested against strains of Pseudomonas aeruginosa (BCRC 11733), Bacillus subtilis (BCRC 10029), Staphylococcus aureus (BCRC 11863), and Escherichia coli (BCRC 11758). Penicillin G potassium salt (CAS 113-98-4, USP grade) was used as a reference medication. Compound 13 showed the highest potency against Bacillus subtilis among the investigated compounds, with a minimum inhibitory concentration (MIC) of 8 μg/ml.[45] in



(13)

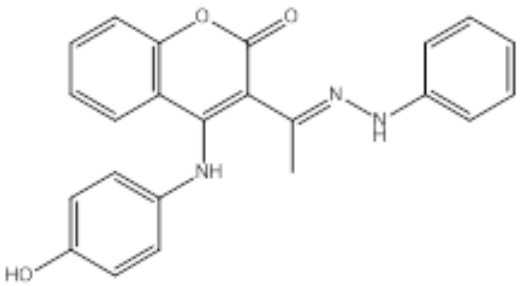
Novel 1,3-dipolar cycloadducts of 3-azidoacetylcoumarins have been successfully synthesized by Kusanur and colleagues using dimethyl acetylene dicarboxylate (DMAD). These recently created compounds' and their adducts' antibacterial activity were thoroughly assessed, with encouraging results. Al-Haiza and his group also generated and evaluated [46] samples of pyridino[3',2'-6,5]-, pyrrolo[3',2'-5,6]-, and [5',4'-6,5]-.Pyrano-4H [3,2-c][1]benzopyran-6-one derivatives for their effectiveness against a range of bacterial strains, including fungi (Aspergillus niger, Penicillium

italicum, Fusarium oxysporum) and Gram positive bacteria (Staphylococcus aureus, Bacillus subtilis, Bacillus cereus) and Gram negative bacteria (Pseudomonas aurignosa, Echerichia coli, and Enterobacter aerogenes). Amoxicillin and mycostatin, typical medications for bacteria and fungi, respectively, were used at a concentration of 1000 ppm to guarantee reliable comparisons. It is worth noting that compound number fourteen had remarkable antibacterial activity against Enterobacter aerogenes.[47]



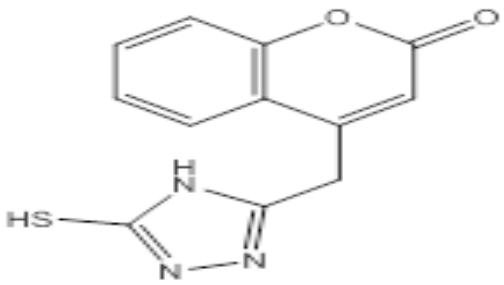
(14)

In a work by Vaso et al., they synthesized numerous novel derivatives at doses of 2 mgml–1, 3 mgml–1, and 5 mgml–1 of 2H-[1]-benzopyran-2–one (coumarin). The antibacterial activity of these substances was subsequently evaluated against three distinct bacterial cultures: Escherichia coli and two Gram positive bacteria, Staphylococcus aureus and Bacillus aureus. The outcomes were contrasted with those of Cephalexine and Streptomycine, two common antibiotics. Compound 15 demonstrated more antibacterial action against Staphylococcus aureus than Cephalexine, but lesser activity against Streptomycine.[48]



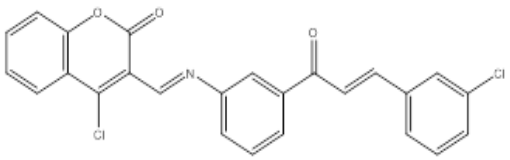
(15)

When Cacic et al. synthesized derivatives of (7-hydroxy-2-oxo-2H-chromen-4-yl)-acetic acid hydrazide (16), they discovered that Staphyloccocus pneumoniae was very susceptible to their antibacterial action. In comparison to the normal medication, these compounds exhibited slightly lower levels of activity against Pseudomonas aeruginosa, Bacillus subtilis, Bacillus cereus, and Salmonela panama.[49]



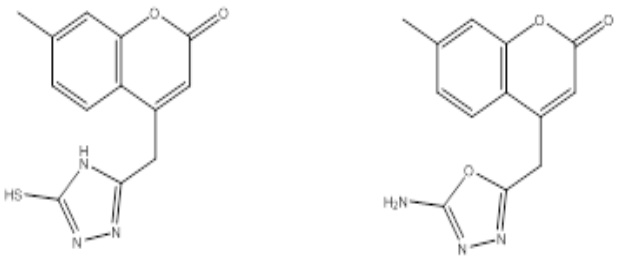
(16)

Schiff's bases, namely 3-(4-(4-(substituted phenyl)prop-1-ene-3-one)phenylimino) methyl)-4-chloro-2H-chromen-2-ones, were synthesized by Kudale et al. The gram positive bacteria Staphylococcus aureus (ATCC 9144), Bacillus subtilis (ATCC 6633), and Staphylococcus epidermis (ATCC 12228) as well as the gram negative bacteria Escherichia coli (ATCC 25922), Salmonella typhi, and Psuedomonas aeruginosa (ATCC 9027) were tested in vitro using these compounds. Moreover, the antifungal activity of these compounds was assessed against two reference medications for antibacterial and antifungal activities, respectively, Aspergillus niger (ATCC 10594) and Clostridium albicans (ATCC 10231). These standard drugs were amoxicillin and fluconazole. Compound 17 had the highest level of activity among all the investigated compounds, with a minimum inhibitory concentration (MIC) of 20μgml–1.[50]



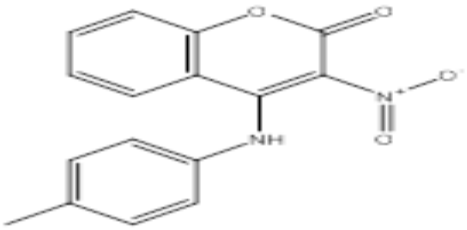
(17)

Bis[N-(4-oxocoumarinylmethylene)]-1,4-di-amines were synthesized by Hamdi et al. and their antibacterial activity was evaluated against Staphylococcus aureus (ATCC 25923) at a concentration of 106CFCml–1 on a Mueller-Hinton agar plate. The chemical with the most potent antibacterial activity was one.[51] Mashelkar et al. synthesized new 4-substituted coumarins and tested them against Salmonella typhi and Gram positive and negative Staphylococcus aureus in vitro. The typical medications were trimethoprim and ampicillin. Significant antibacterial activity was demonstrated by two compounds (18a-18b) against Staphylococcus aureus and Salmonella typhi at doses ranging from 10 to 200μgml–1.[52]Dekic and colleagues produced and assessed 4-arylamino-3-nitrocoumarins.



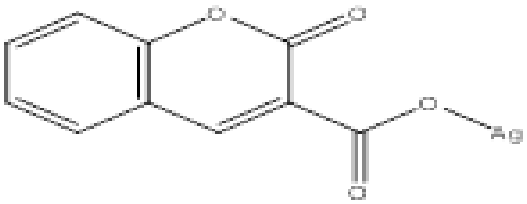
(18a) (18b)

Salmonella enterica (ATCC 13076), Klebsiella pneumoniae (ATCC 10031), Aspergillus niger (ATCC 16404), and yeast Candida albicans (ATCC 10231). Among the compounds in the series, compound 19 demonstrated the highest anticandidal activity. The reference medications were nystatine and tetracycline.[53]



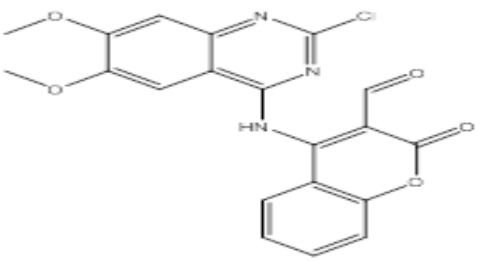
(19)

A number of novel carboxylate ligands generated from coumarin, together with their silver(I) complexes, were synthesized and described by Creaven et al. Following that, these substances were tested for their antifungal and in-vitro antibacterial activities against a variety of Gram positive and Gram negative bacteria. A number of the Ag(I) complexes exhibited strong antibacterial activity, although the ligands themselves showed no such activity. Ag(I) complexes of hydroxy-substituted coumarin carboxylates in particular showed strong activity.[54]



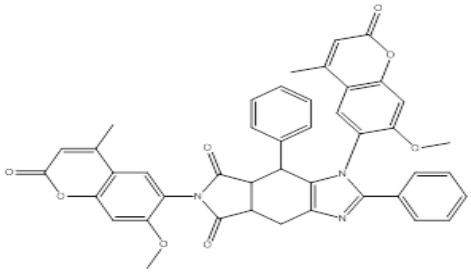
(20)

Researchers produced 4-Heteroaryl-coumarin-3-carbaldehydes and examined their antibacterial activities against a range of bacteria, including Pseudomonas aeruginosa, Hafnia alvei, Escherichia coli, and Enterobacter cloacae, in the study done by Govori et al. Using the Agar disc diffusion technique, the inhibition zone surrounding the agar discs that were soaked in N,N-DMF solution of the compounds at doses of 1, 3, and 5 mg/ml was evaluated. One particular chemical (21) was found to have stronger antibacterial efficacy against Staphylococcus aureus, Escherichia coli, and Enterobacter cloaco, but not against Hafnia alvei or Pseudomonas aeruginosa.[55]



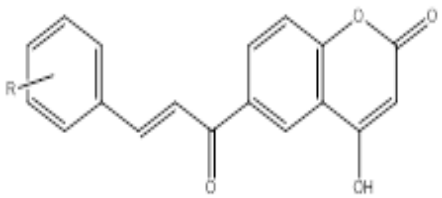
(21)

Mulwad VV et al. produced 4-[1-(2H-[1]-4-hydroxy-2-oxo-benzopyran-3-yl)methylidene] in a different investigation.[1,2,4]triazine-6-one and its derivatives, as well as -2-phenyl-4H-oxazol-5-ones. After screening all of the synthesized compounds for antibacterial activity, it was discovered that they all showed a considerable amount of activity against the tested microorganisms.[56] Furthermore, a unique series of 5H,7H-N-(coumarin-6-yl) was synthesized by Choudhari et al.The antibacterial and antifungal activity of -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 assessed against Salmonella typhi, Clostridium albicans, Aspergillus niger, and Staphylococcus aureus. The substances exhibited antibacterial properties, with minimum inhibitory concentrations (MIC) varying between 50µg and 200µg per milliliter.[57]



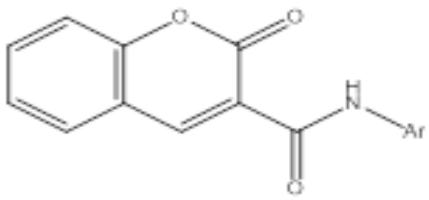
(22)

In order to evaluate the microbiological activity of their newly produced 3-cynnamoyl-4-hydroxycoumarins (23) against a range of bacteria, including Pseudomonas aeruginosa, Echerichia coli, Salmonella typhimurium, Bordatella bronchiseptica, Bacillus subtilis, and Staphyloccocus aureus, Zavrsnik D et al. The compounds containing halogens had the highest levels of microbiological activity; particularly efficient against Bacillus subtilis were those containing 4-Br and 4-Cl, while the most effective molecule against Staphyloccocus aureus was one containing 4-Cl.[58]



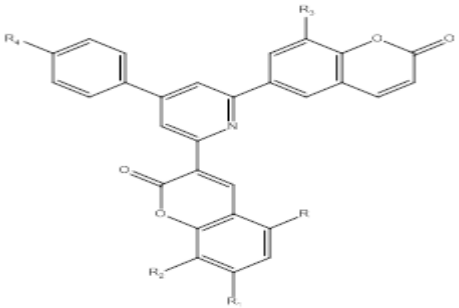
(23)

Similarly, N-substituted-2-oxo-2H-1-benzopyran-3-carboxamides, also known as coumarin-3-carboxamides, were synthesized and tested by Chimenti F et al. as anti-Helicobacter pylori drugs. The compounds with a 4-acyl phenyl group demonstrated the best activity against Helicobacter pylori metronidazole resistant strains, despite the synthesized compounds having little to no activity against different species of Gram positive and Gram negative bacteria and strains of pathogenic fungi.[59]



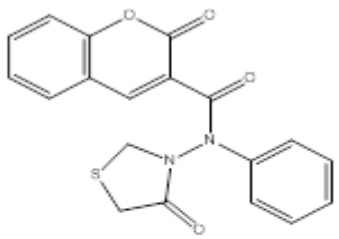
(24)

4-aryl-2,6-di(coumarin-3-yl)pyridines (25) were synthesized by Patel AK et al. and their antibacterial activity was evaluated. Against Aspergillus niger, none of the compounds exhibited antifungal activity. The findings showed that all of the compounds had comparable antibacterial activity and that the presence of substituents such -CH3 or -OCH3 in either the coumarin nucleus or a phenyl ring did not significantly impact the activity. Moreover, the antibacterial activity against Escherichia coli was decreased by the insertion of an additional fused benzene ring between the C-5' and C-6' sites.[60]



(25)

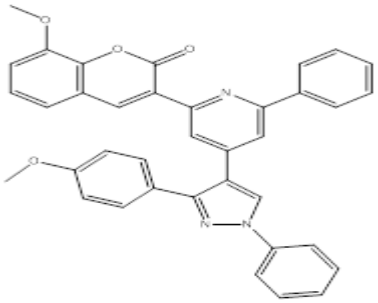
Last but not least, Rama Ganesh et al. created coumarin derivatives with thiazolidin-4-one rings and assessed their antibacterial efficacy against both Gram negative and Gram positive bacteria, such as Escherichia coli and Klebsiella pneumonia. It was discovered that the most active chemical (26) had a 20 mm zone of inhibition against Bacillus subtilis and Staphylococcus aureus.[61]



(26)

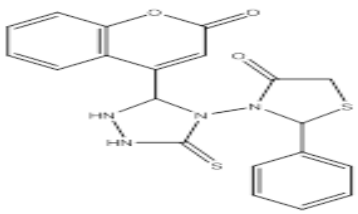
4-methyl-3-phenyl-6-[4-(3-aryl-1-phe¬nyl-1H-pyrazol-4-yl)-6-aryl-pyridin-2-yl]coumarin derivatives (27) were synthesized by Brahm Bhatt et al. and screened using the agar cup diffusion method for antibacterial activity against Escherichia coli and antifungal activity against Candida albican. DMF was utilized as a blank, 1000 µgml–1 concentrations of streptomycin and clotrimazole were used as anti-bacterial and anti-fungal standard drugs,

respectively. When compared to a normal medication, the synthetic compounds exhibited lower levels of activity against both gram positive and gram negative microorganisms.[62]



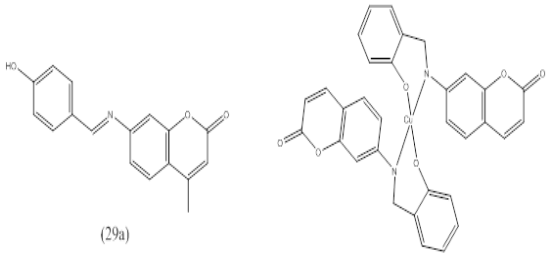
(27)

A series of 2-(substitutedphenyl)-3-[3-(2-oxo- 2H-coumarin-3-yl)] was synthesized by Bhatt et al.The compound 5-thioxo-1,5-dihydro-4H-1,2,4-triazol-4-yl-1,3-thiazolidin-4-ones and evaluated their antifungal and antibacterial efficaciousness against Clostridium albicans and Gram-positive and Gram-negative strains of Escherichia coli. For comparison, the common antibacterial medication ciprofloxacin and the antifungal medication ketoconazole were used. A concentration of 100µg/mL was used to evaluate the test substances and reference medications. DMF, or N,N-dimethylformamide, served as both the solvent and the control. In comparison to Staphylococcus aureus, Escherichia coli, and Clostridium albicans, compound 28 demonstrated growth suppression of 92%, 80%, and 90%, respectively.[63]



(28)

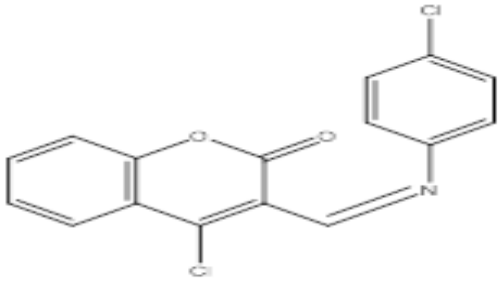
Cu(II) complexes and a sequence of Schiff bases were synthesized by Creaven et al. (29a-29b). All of the free ligands and their metal complexes were compared to amphotericin B and ketoconazole for their antifungal activity. When compared to their respective reference medications, several of the metal complexes exhibited strong antibacterial activity, but the ligands themselves showed little antimicrobial action.[64]



(29a) (29b)

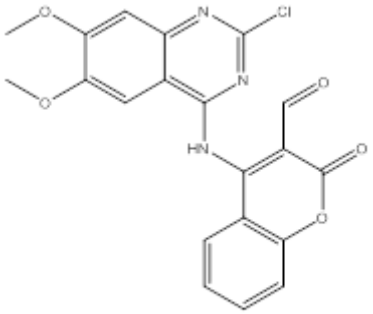
In vitro tests were conducted by Bairagi et al. to evaluate the antimicrobial activity of 4-chloro-3-((subst it ut ed-phenylimino)methyl)-2H-chromen-2-ones against Gram positive bacteria, Bacillus subtilis (ATCC 2063), and Gram negative bacteria, Escherichia coli (ATCC 20931), as well as fungi, Aspergillus niger (ATCC 16404) and Candida

albicans (ATCC 10231). Compound 30 showed the maximum activity, with a minimum inhibitory concentration of 15 µg/ml, against all tested species. The conventional medications for their antibacterial and antifungal properties were amoxicillin and fluconazole, respectively.[65]



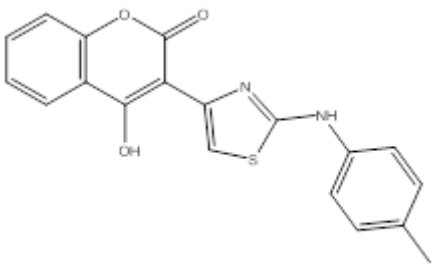
(30)

The Agar disc diffusion technique was utilized to measure the diameters of the inhibition zone surrounding discs that had been previously wetted with N,N-DMF solution of compounds at concentrations of 1, 3, and 5 mg/ml. This allowed for an evaluation of the compounds' activity against Hafnia alvei, Pseudomonas aeruginosa, Enterobacter cloacae, Staphylococcus aureus, and Escherichia coli. Compound 31 shown greater antibacterial efficacy against Enterobacter cloacae, Escherichia coli, and Staphylococcus aureus, but not against Hafnia alvei or Pseudomonas aeruginosa.[66]



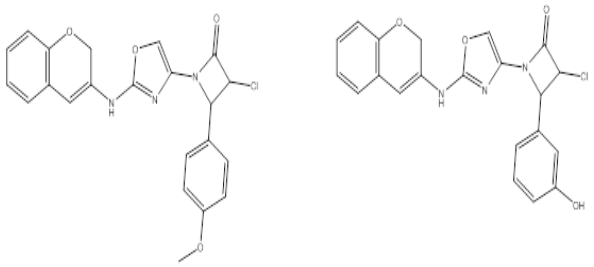
(31)

The authors, Mladenovic et al., synthesized novel derivatives of 4-hydroxy-chromene-2-one and screened them for antibacterial activity against Escherichia coli, Bacillus subtilis, and Gram positive and negative bacteria, Staphylococcus aureus, as well as for antifungal activity against M. mucedo and Candida albicans. For comparison, the antifungal medicine ketoconazole and the common antibacterial antibiotic streptomycin were utilized. Compound 32 demonstrated efficacy against M. mucedo equivalent to that of the reference medication ketoconazole (31.25 µg/ml).[67]



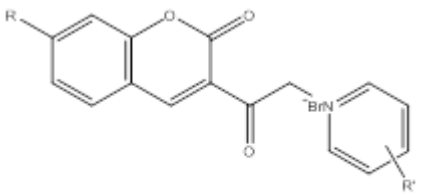
(32)

Singh et al. synthesized a novel series of 3-[(2'-Substituted benzylidene amino thiazol-4'-yl) amino]coumarins (33a–33b), which were then tested against a range of bacteria, including Staphylococcus aureus 209 P, E. Coli ESS2231, Proteus vulgaris, and K. Pneumoniae, to determine their antibacterial properties. Additionally, Candida albicans ATCC10231 was used to evaluate their antifungal activities. The acquired results were compared to those of fluconazole for antifungal activity and those of ciprofloxacin and gattifloxacin for antibacterial activity. The group under control received treatment with propylene glycol. Among the compounds, one was notable for its strong antibacterial activity, while the other chemical showed the strongest antifungal activity.[68]



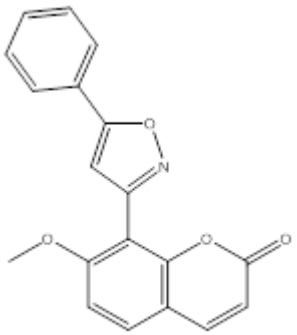
(33a) (33b)

By reacting methyl and ethyl esters of nicotinic acid with isonicotinic acid, Porwal B et al. created 3-coumrinoyl pyridinium bromides (34) and 3-coumarinoyl quinolinium bromides (33) by reacting methyl and ethyl esters of nicotinic acid with quinoline. When compared to the antibacterial activities of gentamycin and amoxicillin, the majority of the investigated compounds had notable antimicrobial activity. utilizing an ELISA reader, the test compounds exhibiting strong qualitative antimicrobial properties were subsequently selected for a quantitative antimicrobial investigation utilizing a 96-well plate and the two-fold dilution technique. It was discovered that the coumarinoyl pyridinium salts with the following properties were more active than the other test compounds: R = -H & R' = 4-COOC2H5, R = -Cl & R' = 4-COOC2H5, R = -H & R' = 3-COOC2H5, and R = -Cl & R' = 4-COOCH3.[69]



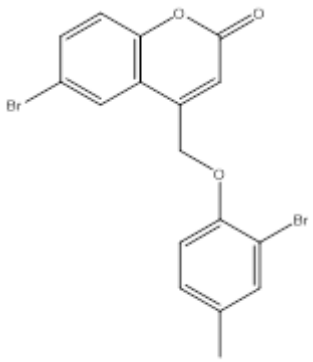
(34)

Sandeep et al. created a novel series of 7-methoxy-4-methyl-8-[5-(substituted aryl)isoxazol-3-yl]–2H–benzopyran-2-ones. Pseudomonas aeruginosa, Bacillus subtilis, Staphylococcus aureus, and Escherichia coli cultures were used to investigate the compounds' antibacterial properties. Additionally, Aspergillus niger, Aspergillus flavus, and Candida albicans were among the fungi that were evaluated. Tested chemicals were tested against all species at 25µg/ml in dimethylformamide. For antibacterial and antifungal activity, standard medicines were ciprofloxacin (25µg/ml) and fluconazole (25µg/ml), respectively. One compound (35) out of those evaluated for antibacterial activity showed the maximum zone of inhibition against S. aureus and B. subtilis and the lowest zone of inhibition against E. coli and P. aeruginosa. The action of the remaining chemicals was moderate.[70]



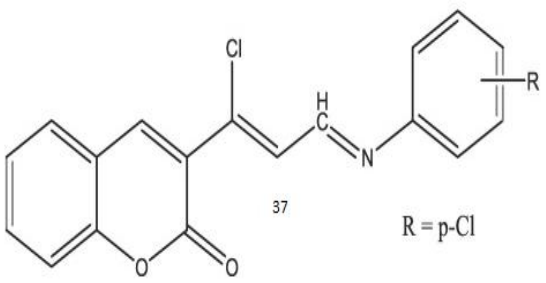
(35)

Basanagouda and colleagues (36) produced 4-aryloxmethylcoumarins and used the disc diffusion method to screen for antibacterial and antifungal activity at various doses (500, 250, 100, and 50 µg/ml). The antibacterial activity was evaluated against three Gram-negative bacteria (Klebsiella pneumonia, Psuedomonas aeruginosa, and Escherichia coli) and two Gram-positive bacteria (Streptococcus faecalis and Staphylococcus aureus). Conversely, five fungi—Aspergillus flavus, Aspergillus fumigatus, Candida albicans, Penicillium notatum, and Rhizopus—were used to assess the antifungal activity. The standard antibacterial and antifungal medications used were ciprofloxacin and fluconazole, respectively. It was discovered that compounds with methoxy, chloro, or bromo substituents at the coumarin's C-6 position had antibacterial and antifungal properties.[71]



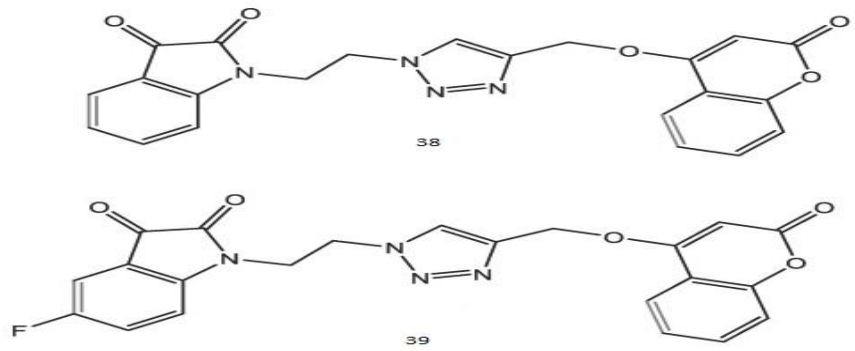
(36)

Kumbar and colleagues synthesized new coumarin Schiff bases and then tested them for biological activity. Every chemical showed a significant amount of action. Compound 37 had significant anti-tubercular efficacy against M. tuberculosis (H37Rv), outperforming the conventional medication isoniazid, which has a MIC value of 0.02 µg/ml. Compound 37's MIC value was less than 2 µg/ml. The presence of a chloro group at the para and meta locations of the phenyl ring is responsible for this increased activity (Kumbar et al.,).[72]

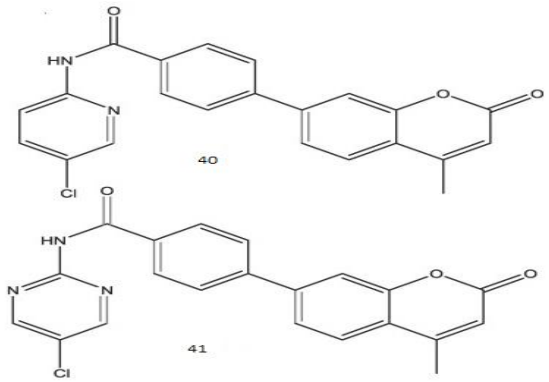


37 R = p-Cl

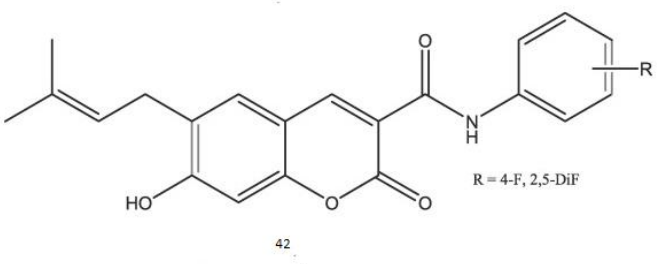
Recently, Bhagat et al. created new derivatives of indolinedione-coumarin and tested them against a range of bacterial and fungal strains to determine their antibacterial capabilities. Compounds 4 and 5 had the most antibacterial activity of all the compounds, with MIC values of 30 and 312 µg/mL, respectively. According to research on structure-activity connections, the length of the carbon chain and the electronic environment have an impact on antibacterial activity (Bhagat et al.).[73]



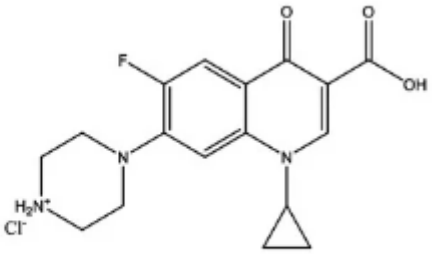
Compound 1's increased antibacterial activity can be explained by the combination of a fluorine group and a pyrimidine ring. Compounds 2 and 3 have antibacterial action in part due to the existence of a heterocyclic ring carrying nitrogen and a chloro substituent.[74]



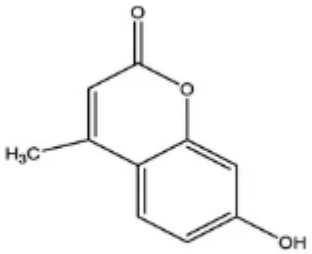
Phutdhawong and colleagues synthesized new coumarin-3-carboxamides and assessed their potential anti-tumor effects. Compound 10 showed the greatest activity of all the compounds against the HepG2 and HeLa cancer cell lines, with IC50 values ranging from 2.62 to 4.85 µM and 0.39 to 0.75 µM, each. The existence of a fluorobezamide moiety is responsible for this increased potential (Phutdhawong et al.).[75]



Novel coumarin compounds were synthesized by Mohamed S. El-Attar et al., who then screened them for antibacterial properties. Additionally, complexes containing these substances were created with three strains of bacteria that are Gram-positive (Bacillus subtilis, Brevibacterium otitidis, and B. cereus) and three strains that are Gram-negative (Escherichia coli, Pseudomonas aeruginosa, and Klebsiella pneumoniae). DMSO-d6 was used to create the testing solutions (El-Attar et al.).[76]



44



43

CONCLUSION

The remarkable biological traits of coumarins have attracted a great deal of study. Due to their physiological, bacteriostatic, and anti-tumor qualities, these compounds are attractive candidates for more research into backbone derivatization and screening as possible therapeutic agents. The anticancer efficacy of coumarin and its metabolite 7-hydroxycoumarin against a variety of human tumor cell lines has been demonstrated by researchers Weber et al. Furthermore, coumarin and its derivatives have shown encouraging promise in several cancer cell lines as inhibitors of cellular proliferation. There is a great deal of interest in creating new antimicrobial compounds since the compounds have a variety of biological actions and their structures allow for different substitutions.

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