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The Evolution of Chromene as Bioactive Molecule

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Abstract

Among the vast range of benz-fused, heterocyclic compounds oxygen-containing compounds occupy a unique position due to their extensive pharmaceutical significance. Particular "Chromene" is well distributed in biologically active molecules and natural products. Chromene has been studied more than five decay and has usually been isolated from natural products often from plants and roots. They are important precursors of biologically active benzopyrans, which exhibit a broad spectrum of potent biological activities including antioxidants, antimicrobial, anti-inflammatory, antiproliferative, antitumor, antimalarial, anticancer, and anti-HIV.

Keywords: Chromene, pyran, biological activity

Introduction

In last 75 years Heterocyclic compounds have a large range of applications in medicinal, agriculture, and materials chemistry[1]. The heterocyclic compounds have been an interesting field of study for a long time. They are broadly distributed in nature, playing a crucial role in living animals. Statistically, more than 85 percent of all biologically active compounds are heterocycles or comprise heterocycles. Heterocyclic molecules are the fundamental building blocks of biological systems. Heterocycles are present enormously in drugs[2], vitamins[3], many natural products[4], biomolecules[5], and active biological compounds such as antineoplastic[6], anti-inflammatory[7], antidepressant[8], antimalarial[9], anti-HIV[10], antimicrobial[11], antifungal[12], antiviral[13], antidiabetic[14], herbicidal[15], and fungicidal agents[16]. In addition to these, the heterocycles are often found as a lead compound in drug synthesis and agrochemicals. Some of these molecules show solvatochromic[17], photochromic[18], and fluorescent properties[19].

Discussion

Some synthetic bioactive chromene derivatives

Chromene as antihypertensive agent-

Several chromenes are known to possess antihypertensive activity, one of the most antihypertensive chromenes reported is the 2,2-dimethyl chromene derivative 1[20]. The 6-nitro derivative of 1 and 6-cyano analog of 2 showed maximum activity. The 2-pyridone substituent at C-4 was also found to be important for antihypertensive activity. Other chromene classifications found to possess antihypertensive activity include the 6-cyano derivative of 4-pyrazinone 2 and structure 3 also shows good antihypertensive activity.

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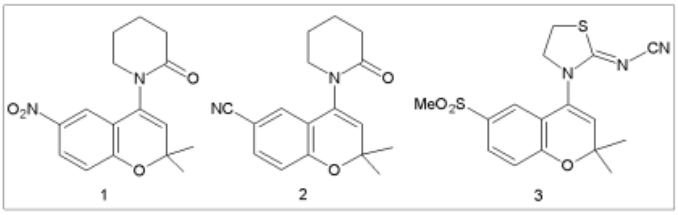

Figure 1- Chromene as antihypertensive agents

Chromene as anti-implantation agent-

The synthesis of the 3,4-diaryl-chromene derivative has been accomplished by treating different 3,4-diaryl-coumarins with an excess Grignard reagent to achieve the corresponding diols, thermal cyclization of which affords the predictable chromenes. The structure-activity of these analogs was performed by Ray and group, the para-hydroxy analogs 4 showed inactivity against anti-implantation, an ether moiety at the para position of the 4-phenyl as in compound 5 was found to be crucial for anti-implantation activity. The removal of the 7-methoxy group from compound 6, decreased the activity, while due to replacement of the germinal methyl substituent as C-2 led to an increase in the activity[21].

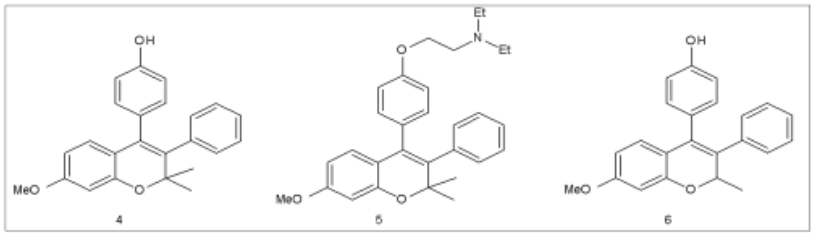

Figure 2- Chromene as anti-implantation agent

Chromene as antineoplastic agents-

4-aryl substituted coumarins 7 were synthesized and tested for anticancer property[22]. Novobiocin analogs 8 were tested by Bras and group as antiproliferative managers and found effective against carcinogenic cells[23]. The chromene 9 exhibited good activity in the nanomolar range for the non-small-cell lung cancer cell lines. The compound 10 interfered with protein kinase B induced apoptosis via the intrinsic pathway and inhibited estradiol-induced hyperplasia formation in rat uterus. The 4*H*-chromene compound 11, was examined for cytotoxicity and the substitution having R_1, R_2= ethyl, and R_3 =H was found to act as an antagonist, representing selective cytotoxicity toward malignant cells[24].

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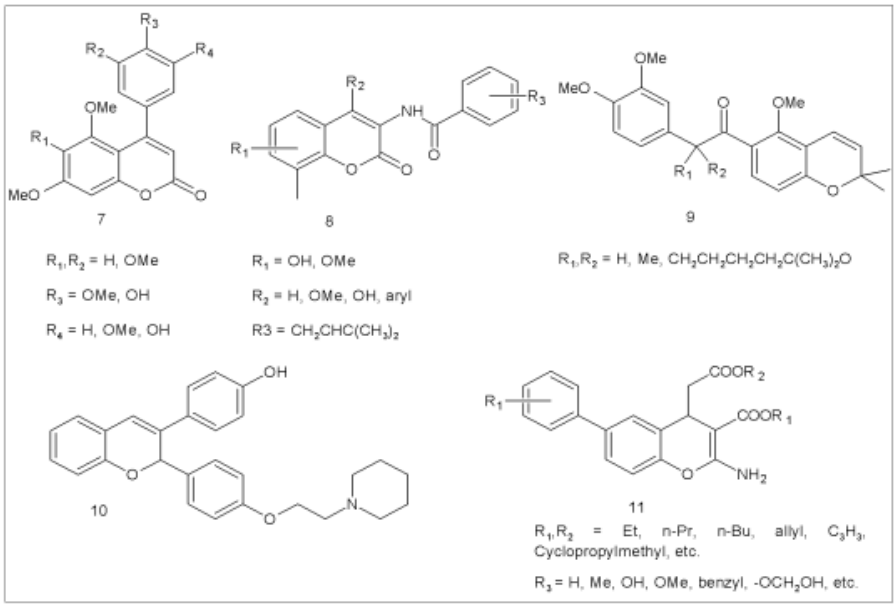

Figure 3- Chromene as an antineoplastic agent

Chromene as antibacterial and antiviral agents-

The antibacterial agents continue to be significant owing to the prevalence of bacterial infection. The antibacterial activity of chromene 12 was determined by agar diffusion methods against gram-negative *Escherichia coli* and gram-positive *Staphylococcus aureus* strains. Compared to *streptomycin* these chromene compounds showed modest antibacterial activities. Chromene derivatives 13 and 14 were tested against different bacterial strains[25].

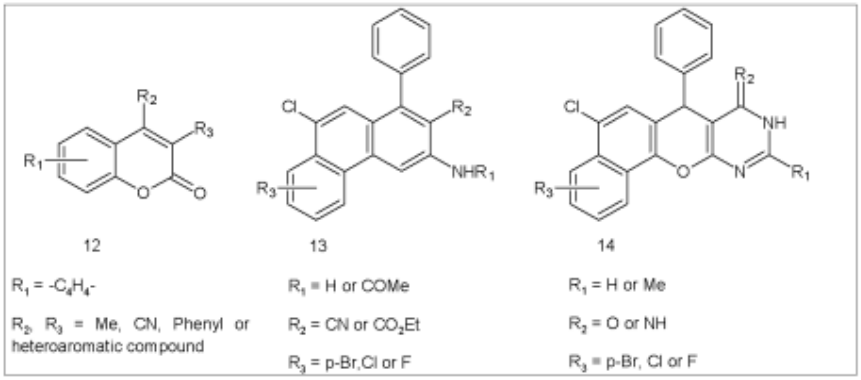

Figure 4- Chromene as antibacterial agent

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Compounds 15-17 were prepared and tested for their anti-HIV activity. Benzo[c]chromene 15 were faintly active on HIV aspartic protease with IC_{50} values from 10 to 50 μM[26]. Calanolide A derivative compound 16 showed excellent activity against HIV, particularly when R_1 and R_2 = H or chloro-substituents.

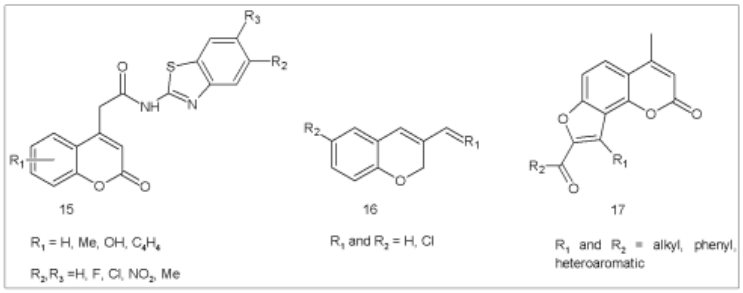

Figure 5- Chromenes as antiviral agent

Chromene as anti-inflammatory agents-

Nicolaides and their research group synthesized and tested for the anti-inflammatory and antioxidant activities of benzo-chromene derivatives[27]. All the synthesized compounds were tested for their antioxidant activity by DPPH methods and showed good antioxidant activity with efficient IC_{50} results. Coumarin derivatives 18-21 were exposed as strong hydroxyl radical scavengers and competing with dimethyl sulfoxide. Fused dioxolane-coumarin derivatives 22 and 23 were examined for their anti-inflammatory and antioxidant activity.

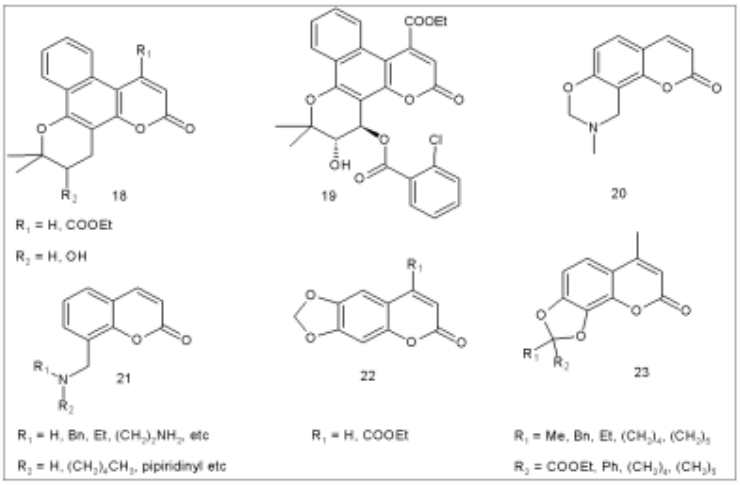

Figure 6- Chromene as an anti-inflammatory agent

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Chromene as anti-diabetic agents-

Rina Soni and her team found the anti-diabetic activity of various chromene-2-one derivatives. DPP-IV inhibitors have been studied as promising pathways to treat Type 2 diabetes and compounds 24 and 25 showed good inhibitions at 10μM concentration[28] by comparing inhibition with sitagliptin and vildagliptin which are well known DPP-IV inhibitors.

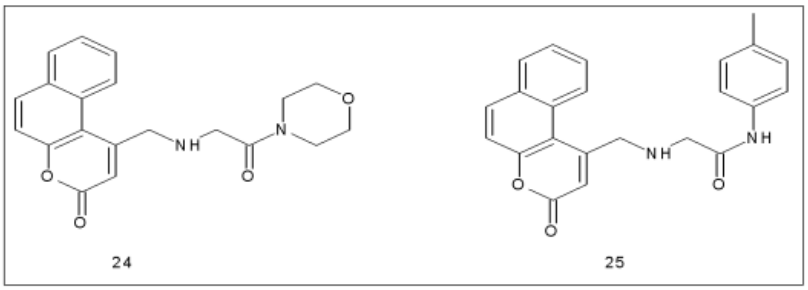

Figure 7- Chromene as antidiabetic agen

Chromene as antifungal agents-

According to Sawsan A. Fouad and research group chromene-2-one, pyrano[3,4-c]chromene 26 showed equipotent potency of the standard antifungal drug in inhibiting the growth of *S. pyogenes* (MIC 0.24 μg/mL) and *P. vulgaris* (MIC 1.95 μg/mL). Pyridino[3,4-c]chromene 27 showed equipotent potency of the standard drug in inhibiting the growth of *A. Fumigates* (MIC 0.97 μg/mL) and *P. marneffei* (MIC 1.95 μg/mL)[29].

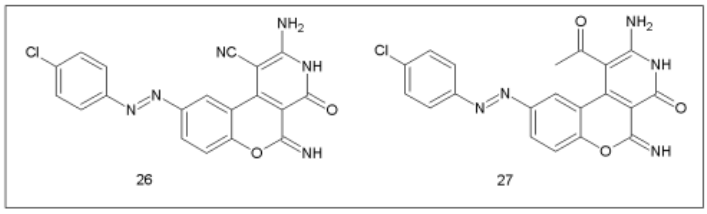

Figure 8- Chromene as an antifungal agent

Conclusion

Chromene derivatives were synthesized by many methods generally by condensation of various aromatic aldehydes and active enol group like coumarin using suitable catalyst in proper solvent. These types of chromene derivatives show the variety of pharmacological activity towards physiological functions of human being. These types of compounds have tremendous scope as lead compound for drug development through structure activity relation.

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