Review Article

Coumarin-Chalcone Hybrids for Biological Potentials: A Strategy of Molecular Hybridization for Drug Design

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ABSTRACT

Naturally and synthetically originated hybrid molecules are promising sources for new drug development due to their multiple advantages like high efficacy, mode of action at receptors minimum side effects and better pharmacokinetic properties. Coumarin and chalcone, are important classes of synthetic chemistry affording diverse pharmacological activities, make themselves ideal blocks for building a coumarin–chalcone hybrid scaffolds as a bioactive agents. Provoked by the promising medicinal and therapeutic applications of such hybrids, the scientific community has reported dozens of coumarin–chalcone hybrids with a wide spectrum of biological properties including anticancer, antimicrobial, antimalarial, antioxidant, antiviral, anti-inflammatory analgesic, antianxiety and so on, through synthetic hybridization strategy. It is expected to assist medicinal chemists in the effective and successful development of coumarin–chalcone hybrids for their biological potentials. In view of these observations, we herein report the some literature review of coumarin-chalcone hybrids which possessing antimicrobial, anticancer, antiviral, antimalarial and antioxidant potential.

Keywords: Coumarin, Chalcone, Molecular hybridization, Biological potentials.

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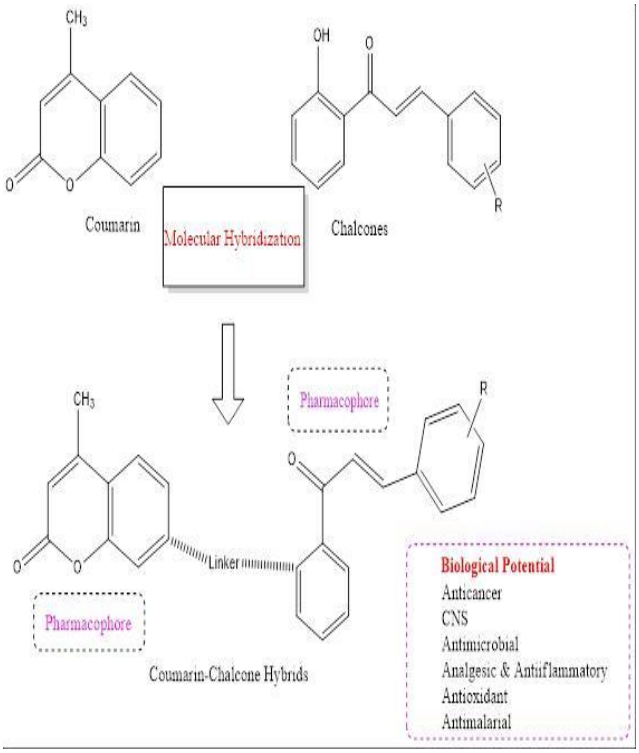
GRAPHICAL ABSTRACT



INTRODUCTION

Chromene (benzopyran) is one of the privileged medicinal pharmacophores, which appears as an important structural component in natural compounds and has generated great attention because of its interesting biological activities including antimicrobial action. Chromene constitutes the basic backbone of various types of polyphenols and is widely found in natural alkaloids, tocopherols, flavonoids, and anthocyanins. It is known that certain natural and synthetic chromene derivatives possess important biological activities[1-5]. Chalcone is an aromatic ketone and an enone that forms the central core for a variety of important biological compounds, which are known collectively as chalcones or chalconoids.

Chalcones can be prepared by an aldol condensation between benzaldehyde and acetophenone in the presence of sodium hydroxide as a catalyst. Chalcones are active lead molecules in medicinal chemistry for the discovery of new drugs. Chalcones have been reported to possess many useful biological properties including antimicrobial, anti-inflammatory, anticancer and antioxidant activities[6-10]. In view of these biological significances of coumarin and chalcones, a strategy of synthetic molecular hybridization between coumarins with chalcones is used to design number of coumarin-chalcone hybrids for therapeutic potentials by scientific community. Here, we are citing of number of literatures of coumarin-chalcone hybrids for therapeutic potentials.

LITERATURE REVIEW

Coumarin-Chalcone hybrids

Tandel HT *et al.,* (2019) synthesized novel coumarin-chalcone hybrids and screened for in vitro antimicrobial activity against selected pathogens[11] (Fig: 1).

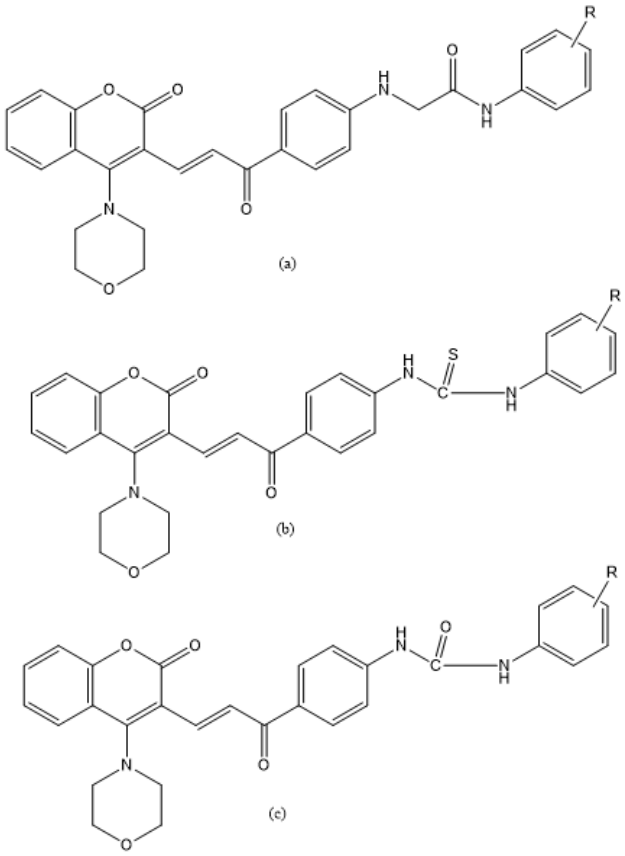


Figure 1: Coumarin-Chalcone hybrids (a, b, c).

Kurt B Z *et al.,* (2017) reported a structure-based molecular hybridization approach, and series of novel coumarin-chalcone derivatives containing urea moiety was synthesized and screened for their *in vitro* antiproliferative activities against the cancer cell lines (H4IIE and HepG2) [12] (Fig: 2).

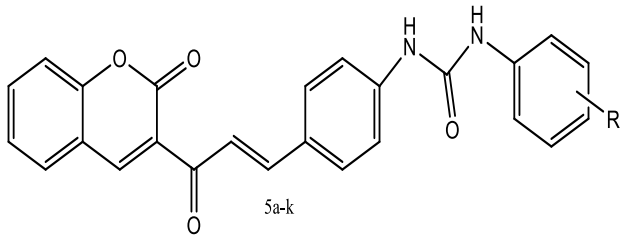


Figure 2: Cytotoxicity activities of the synthesized compounds (5a-k) against H4IIE, HepG2 and CHO cells *in vitro*.

Mukusheva G K *et al.*, (2015) reported the flavanone pinostrobin in the synthesis of coumarin-chalcone hybrids with a triazole linker[13] (Fig: 3).

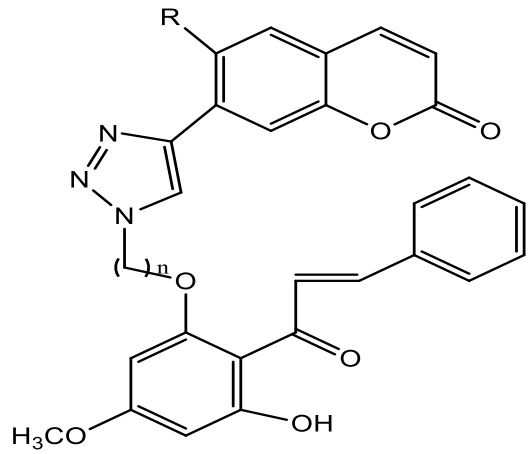


Figure 3: Coumarin-chalcone hybrids containing a triazole linker.

Dongamanti A *et al.,* (2014) reported a new series of hybrid compounds containing coumarin, 1, 2, 3-triazole, and chalcone substructures were synthesized and screened for their antimicrobial activity[14] (Fig: 4).

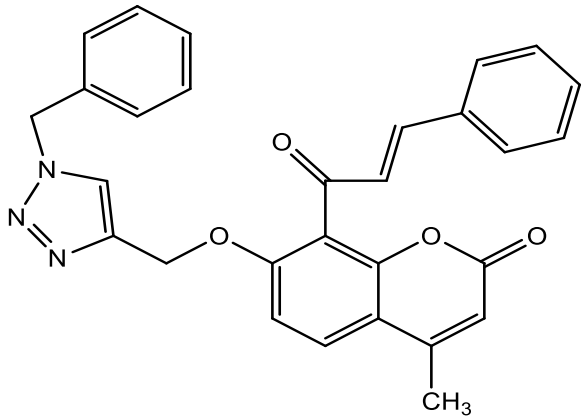


Figure 4: Coumarin-chalcone hybrids containing a triazole.

Perez-Cruz F *et al.,* (2015) reported synthesis and electrochemical and biological studies of novel coumarin−chalcone hybrid compounds[15] (Fig: 5).

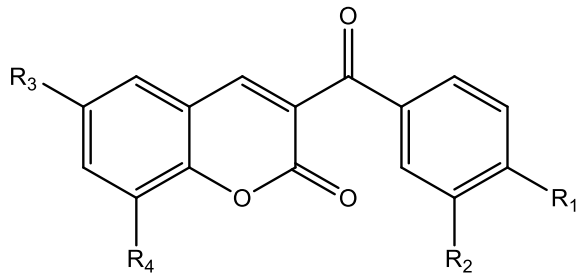


Figure 5: Hydroxy-coumarin-chalcone hybrid compounds.

Moodley T *et al.,* (2016) reported the synthesis and antibacterial activity of 2- and 4-substituted-coumarinyl chalcones and explored the effect that chloro, fluoro, hydroxy, methoxy and phenyl groups have on activity as well as determined which of the 2 or 4-position were better for substitution with regards to antibacterial activity[16] (Fig: 6).

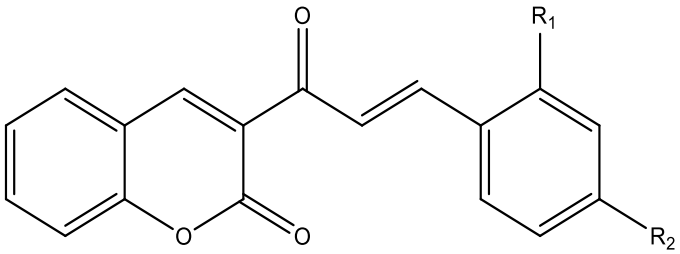


Figure 6: 2- and 4-substituted-coumarinyl chalcones.

Spirtovic-Halilovic S *et al*., [2014] reported the *in vitro* and *in silico* experiments for screening the antibacterial activity of coumarin-chalcone hybrids (7a-d). The *in silico* studies explain the stability and reactivity of hybrids[17] (Fig: 7).

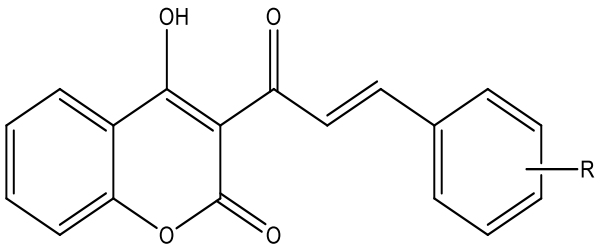


Figure 7: Coumarin-chalcone hybrids (7a-d).

Deshpande HA *et al.,* [2013] reported the antibacterial activity of coumarin-chalcone hybrids (4a-g) against five human pathogens. The hybrid (4g) with para chloro substitution on benzyl ring of chalcone shows potent activity against Gram-positive bacteria[18] (Fig: 8).

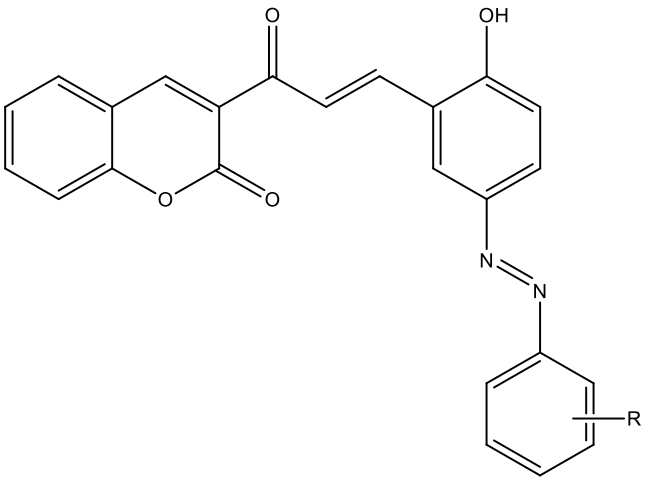


Figure 8: Coumarin-chalcone hybrids (4a-g).

Vazquez-Rodriguez S *et al.,* [2015] reported the antibacterial activity of coumarin-chalcone hybrids for the treatment of tenacibaculosis through disk diffusion assay against general Gram positive and Gram negative and 17 different strains of Gram-negative marine bacteria belongs to *Tenacibaculum* genus using oxolinic acid, enrofloxacin, and ampicillin as controls[19] (Fig: 9).

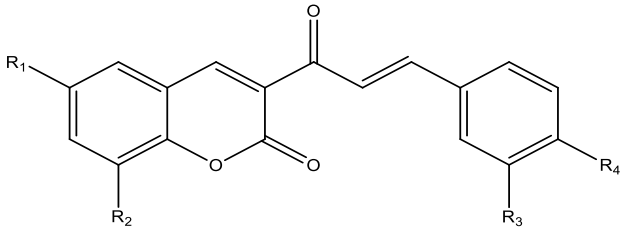


Figure 9: Coumarin-chalcone hybrids (2a-d).

Olea-AzarClaudio *et al.,* [2018] reported the synthesis and antioxidant study of new polyphenolic hybrid-coumarins. The antioxidant capacity of hydroxylated coumarin and hydroxybenzoic acids has been widely described. The new hybrid compound synthesized with acommon coumarin scaffold and hydroxybenzoic acids is described[20] (Fig: 10).

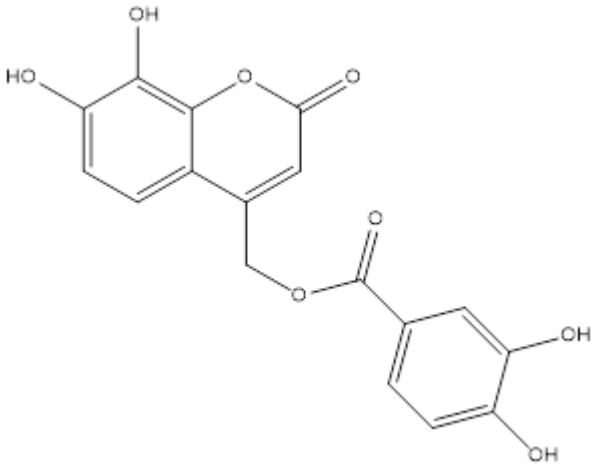


Figure 10: Coumarin and acid derivatives (3a-c) synthetic rout.

Zavrsnik D *et al.,* [2017] reported synthesis of coumarins. The antimicrobial 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 antimicrobial 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*[21] (Fig: 11).

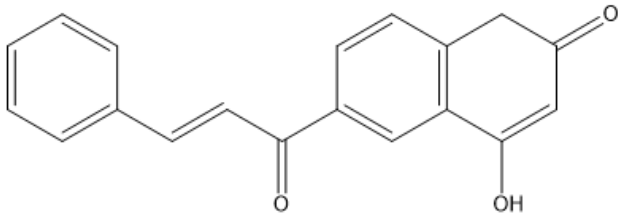


Figure 11: Coumarin hybrid.

Al-Amiery Ahmed A *et al.,* [2017] reported synthesis of coumarins. The antimicrobial activity of a series of the Schiff's bases 3-(4-(4-substitutedphenyl) prop-1-ene-3-one)phenylimino)methyl)-4-chloro-2H-chromen-2-ones. This is using amoxicillin and fluconazole as standard drug for antibacterial and antifungal activities[22] (Fig: 12).

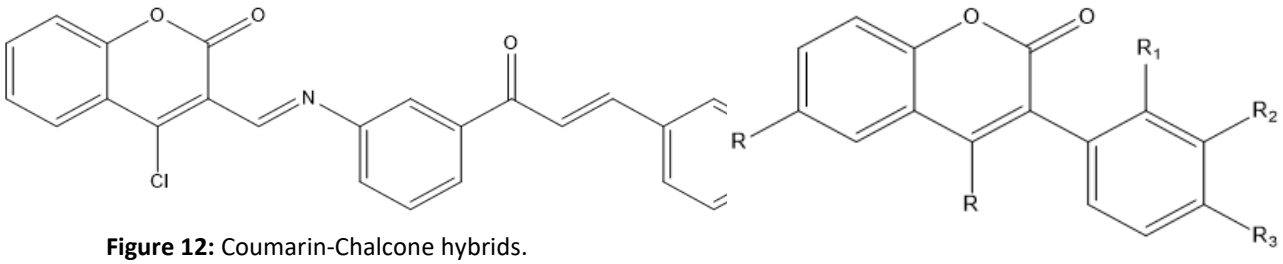


Figure 12: Coumarin-Chalcone hybrids.

Vazquez-Rodriguez *et al.,* [2016] reported efficient synthesis of coumarin-chalcones hybrids as new scaffold with antibacterial interest[23] (Fig: 13).

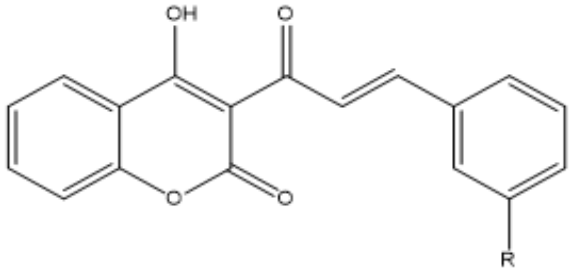


Figure 13: Coumarin-Chalcone hybrids.

Tandel H T *et al.,* [2018] reported the synthesis of antibacterial activity of novel coumarin-chalcone hybrids. Natural and synthetic molecules based on coumarin skeleton have been employed as medicinal agent such as anti-inflammatory, antimicrobial and antimalarial[24] (Fig: 14).

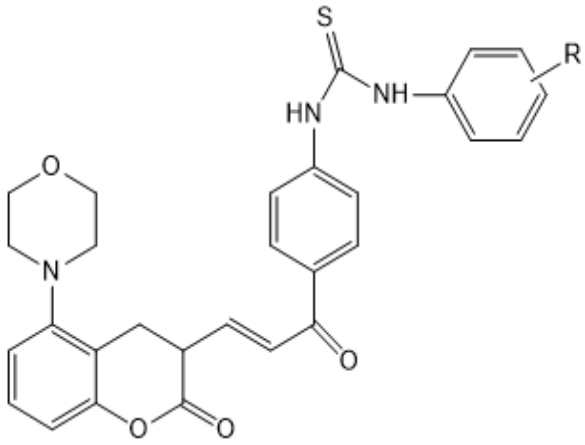


Figure 14: Coumarin-chalcone hybrids (5e-h).

Yasameen Al-Majedy *et al.,* [2017] reported the antioxidant activity of coumarins. Coumarins are heterocyclic molecules that have been associated with beneficial effects on human health, such as reducing the risk of cancer, diabetes, cardiovascular and brain diseases. These effects are thought to be related to the radical scavenging effect, due to their antioxidant activities[25] (Fig: 15).

Figure 15: Coumarin derivatives.

Osman Hasnah *et al.,* [2018] reported the designing, synthesis, characterization, X-ray crystal structure, antibacterial and antiviral evaluations of new thiazolyl-coumarin hybrids[26] (Fig: 16).

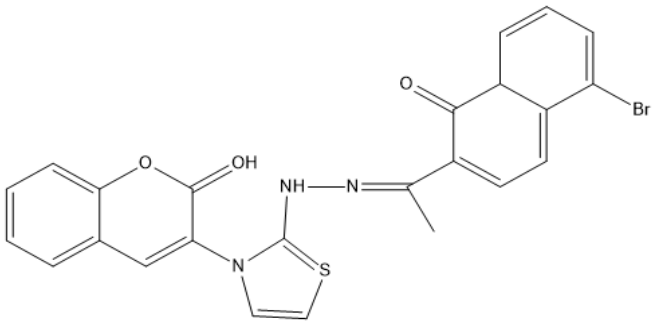


Figure 16: Thiazolyl-coumarin hybrids.

Vazulz-Rodriquez S *et al.,* [2015] reported the synthesis and trypanocidal and antimicrobial properties of new coumarin-chalcone derivatives[27] (Fig: 17).

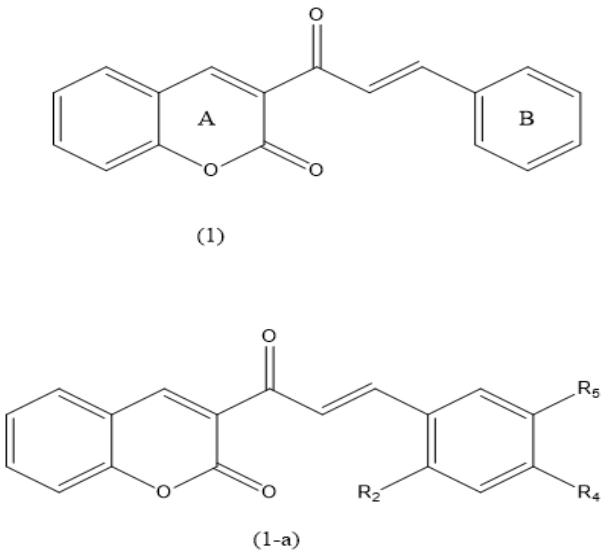


Figure 17: Coumarin-chalcone derivatives (1-a).

Guey-Jen Lee-Chen *et al.,* [2018] reported the novel synthetic coumarin-chalcone hybrid for A-beta aggregation reduction, antioxidation, and neureotection. Alzheimer disease the most common type of dementia among the neurofibrillary tangles in the brain. [28] (Fig:18).

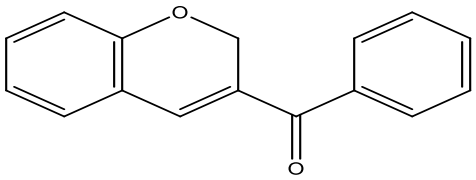


Figure 18: coumarin –chalcone hybrid.

Wenwei Lin *et al.,* [2018] reported the novel synthetic coumarin-chalcone hybrid for A-beta aggregation reduction, antioxidation, and neureotection. [29] (Fig:19).

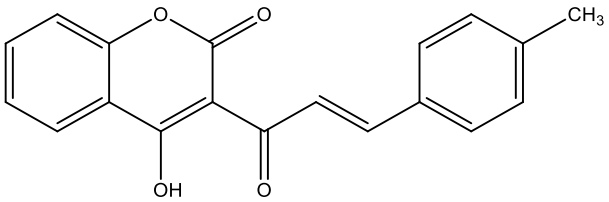


Figure 19: coumarin-chalcone hybrid.

CONCLUSION

The present review paper focused the therapeutic potentials of various coumarin- chalcone hybrids. This literature review is useful for the designing of M.Pharm project work for better understanding of coumarin-chalcone hybrids regarding their characteristic biological activities in the development as therapeutic agents.

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