INTERNATIONAL JOURNAL OF EXPLORING EMERGING TRENDS IN ENGINEERING
Peer-Reviewed, Refereed, Indexed and International Journal, https://ijoeete.com/
|ISSN No. 2394-0573 |Volume: 10, Issue: 2 | July - Dec 2023

"COUMARIN DERIVATIVES HAVING DIFFERENT BIOLOGICAL ACTIVITIES"

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Abstract:
:Coumarin (2H-Chromen-2-one) is a heterocyclic compound having molecular formula C9H6O2 and contains oxygen in its structure. Coumarin belongs to the lactones family having a benzopyrene system. Many coumarinnucleiplay an important role in medicinal chemistry to synthesize a series of various biologicalactive derivatives as anti-inflammatory, antipyretic, antioxidant, bronchodilator, vasodilator, antiamoebic, antibacterial, and antifungal activities. Apart from this, coumarinsalso act as lipid-lowering agents having mild triglyceridelowering activity.Many chemical reactions have been established that can be used to synthesize coumarinslike the Knoevenagel condensation reaction, Perkin, Pechmann reaction, and Reformat sky and Wittig reactions. All the coumarin derivatives are mentioned in the article,these derivatives of coumarin are tested for various pharmacological activities. The main motive of this review article isto describe their pharmacological action and activities against different types of bacteria by using different types of models(invitro assay, in vivo assay,etc).

Keywords::coumarin, chroman, chrome, heterocyclic compounds, Spiro [chromane-2, 4‟piperidine]-4(3H) one, Chroman-4-one.

1. Introduction

2H-Chromen-2-one or 2H-1-benzopyran-2-one (coumarin)is a naturally occurring heterocyclic compound containing oxygen in their structure abundantly present in the different kingdoms of the plant; it was first found in Tonka bean trees (Dipteryxodorata Wild). The history of these natural products started 200 years ago the name of the class derived from the plant Coumarin moderate (Dipteryxodorata) from which coumarin itself (Figure 1) is the simplest member of this family, which was isolated by Vogel in 1820. Chemically, coumarins are organic heterocyclic compounds and their nucleus is represented by benzo-α-pyrone (2H-1benzopyran-2-one), whose systematic nomenclature was established by the International Union of Pure and Applied Chemistry (IUPAC)

Fig.1. Structure of coumarin nucleus.

Coumarin and its derivatives are reported to have a wide spectrum of biological activity [2–5]. Many of these compounds have been proven to be active as antibacterial [6–8], antifungal [9], anti-inflammatory [10], anticoagulant [11], anti-HIV [12], and antitumor agents [13]. Coumarins are extensively used as food additives, perfumes, cosmetics [14], pharmaceuticals, and optical brighteners [15] and would dispersed fluorescent and laser dyes [16].The first time coumarin is reported in 1884 by Pechmann et al.which was first synthesized via the Perkin reaction in 1868 and many simple coumarins are still prepared through this method. In the early 1900s, the Knoevenagel reaction exploits as an important synthetic method to synthesize coumarin derivatives with a carboxylic acid at the 3-position. To date, many other synthetic methods were reported for coumarins, like the Pechmann, Reformat sky, and Wittig reactions[17]. Chromens is a benzopyran ring-containing compound. Benzopyran is a heterocyclic organic compound popular as chromenes that are obtained by the fusion of the pyran ring, which containsan oxygen hetero atom with the benzene ring. A sufficient amount of chromeis found in the bark oil of cinnamon, essential oil, oil of cassia leaf and lavender oil, etc. In the IUPAC

PHARMACOLOGICAL ACTIVITIES:

Antiprotozoal activities:

The analogous of chalcone having a double bond in the side chain between the carbonyl moiety and the phenyl residue was nearly as active as the natural product [18]. The synthetic tricyclic chromene 2 which has the exocyclic benzylidene moiety also showed strong antileishmanialactivity[19]. The medicinal plant Ageratum conyzoides L. (Asteraceae) is used in traditional medicine against numerous diseases including protozoan infections [20]. Recently,

it was reported that the dichloromethane extract of A. conyzoides L. shows significant activity against T. b. rhodesiense[21]. In a search for the active constituents, when tested after total synthesis the chromeneencecalolangelate 3[22] was noticed in the extract but depicted only low anti-trypanosome activity [23]. The stability of the 3 compounds was found to be ultra-low so the weak bioactivity may be related to its rapid degradation when tested as a pure compound. The instability of the 3 compounds begins from the superficial dissociation of the angelate anion since the rest of the benzylic cation is stabilized by two substituents. Thus, when storing the angelate 3 in a methanolic solution a rapid formation of the corresponding methyl ether was detected.

Anticancer and anti-TB activity:

Spiro compounds are investigated for their potential anticancer and anti-TB activity. Some clinically used spiro drugs as potent anticancer and anti-TB agents

Spiro chromanones as Acetyl-CoA carboxylase (ACC) inhibitors: Acetyl-CoA carboxylase (ACC) is examined as an important research area in medicinal chemistry and it is currently a „trending" research topic. It is one of the biotin-dependent homooligomericproteins, responsible for the synthesis of malonyl-CoA from acetyl-CoA in an ATPdependent manner and consists of a biotin carboxyl carrier protein, a carboxyl transferase (CT) and biotin carboxylase (BC) domains. Many companies Merck-Banyu [56a, 57], Takeda [56b], and Pfizer [56c] possess multifaceted Spiro chromanones 25, 26, and, 6 respectively.

Anticancer activity:

A series of 3-benzylidine-4-chromanones 17 were synthesized by Perjésiet al. as cytotoxic agents(Fig. 10). These compounds were examined as oxygen analogs of 2-benzylidene-1- tetralones 16 and tested against Molt 4/C8 and CEM T-lymphocytes as well as murine L1210 lymphoid leukemia cells. In general, 3-benzylidene-4-chromanones 17 were more potent than the corresponding 2-benzylidene-1-tetralones 16. Also, the 3-benzylidene-4-chromanones 17 was reported to have selective toxicity for cancer cells concerning that of normal cells and has been tolerated in mice.

Antitubercular activity:

Roy and colleagues prepared a series of (E)-7-hydroxy-3-benzylidene-chroman-4-one analogs as efflux pump inhibitors against Mycobacterium smegmatis mc2 155. The SAR study demonstrated that the (E)-7- hydroxy-3-benzylidene-chroman-4-one structure is required for efflux pump inhibitory activity. The substation of the hydroxy group at C-5 or C-8 and methoxy group at the C-8 position of the chromanone ring diminish the efflux pump inhibitory activity.

Monoamine oxidase (MAO) inhibitory activity: MAO inhibitors were implemented in the treatment of many psychiatric and neurological disorders. Desideri and colleagues reported a series of homoisoflavonoids as inhibitors of human monoamine oxidase isoforms A and B (hMAO-A and hMAO-B). The evaluation of compounds using the AmplexRedMAO assay kit foundthat compounds 32 and 33 (Fig. 14) were the most potent and demanding hMAO-B inhibitors (IC50 values 8.61 and 8.51 nM, respectively). Their potency was more than that of selegiline (standard drug). The hMAO-B selectivity of both compounds can be related to the different hydrogen bond interactions in hMAO-B active site.

Antibacterial activity:

Jogi et al. have reported the antibacterial activity of novel coumarin-based azo compounds as shown in (Fig.17), synthesized by using hymecromone as a starting material, and exhibited promising antibacterial activity against the test bacteria. Compounds have been found to show an antibacterial activity comparable with ampicillin and streptomycin.

Antioxidant activity:

Šarkanjet al.have reported the synthesis of two series, as shown in (Fig.18), of new five hybrid coumarins, herein termed N18-N22, starting from hymecromone. In the first series, hymecromone was incorporated with thiosemicarbazides, while in the second series, it was incorporated with 4- thiazolidinediones. The chain-breaking ability of these new coumarins was tested versus 2, 2- diphenyl-1-picrylhydrazyl (DPPH) and galvinoxyl free radicals. The authors concluded that the incorporated coumarins of the first series showed better antioxidantactivity than that of the second one. Also, the best activity was contributed to compounds N20 and N21.

Anti-inflammatory potential:

Naik et al. has reported the synthesis of 13 hymecromone-based derivatives. The antiinflammatory impact of the resulting derivatives (Fig.20) was screened by a protein denaturation technique and also studied their QSAR (quantitative structure-activity relationship). The conclusions exhibit that these derivatives have a prominent anti-

inflammatory activity. Also, the authors concluded that various changes in the aromatic ring have a minor impact on this type of activity.

Antiviral potential:

Bishnoi et al. have reported the synthesis of five hymecromone-based derivatives, herein termed N49- N53 (Fig.21), and their antiviral activity was tested versus the RNA virus named Japanese encephalitis virus. The results exhibited that compounds N49 and N52 showed excellent antiviral activity with an inhibition percent of 100. Compounds N50 and N53 have shown a good inhibition percentage of about 75. Only compound N51 has shown poor activity that may be assigned to having weak interactions with the target.

CONCLUSION:

Coumarin (2H-Chromen-2-one) is a heterocyclic compound having oxygen in its structure.Based on various literature surveys Coumarin is reported to have many biological activities such as anti-inflammatory, antipyretic, antioxidant, bronchodilator, vasodilator, antiamoebic, antibacterial, and antifungal activities. This paper includes the various coumarin derivatives such as Spiro [chromane-2, 4‟-piperidine]-4(3H)-one with anti-cancer and anti-TB, Acetyl-CoA carboxylase (ACC) inhibitors activity. 3-benzylidene-4-chromanones with anticancer, antitubercular, antioxidant,monoamine oxidase inhibitors, and diagnostic imaging activities. The SAR study exhibited that for accumulation and efflux pump inhibitory activity,(E)-7- hydroxy-3benzylidene-chroman-4-one structure is essential. The substitution of the hydroxy group at C-5 or C-8 and the methoxy group at the C-8 position of the chromanone ring diminished the efflux pump inhibitory activity. The coumarin-based azo compound hasantibacterial activity. The design of a 3-benzylidene-7-methoxy-4-chromanones-basedstructure isa well-known cytotoxic agent, dibenzofuran-incorporated 3-benzylidene-4-chromanones as antimycobacterial agents. The overall conclusion is that benzopyran has been one of the prosperous heterocycles shown a wide range of biological activities.

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