MEDICINAL SIGNIFICANCE OF NOVEL COUMARINS: A REVIEW

SHARANABASAPPA B. PATIL*, GOURAMMA P., SHIVAKUMAR S. JALDE

*Department of Chemistry, Ramaiah Institute of Technology, Bangalore 560054, Department of Chemistry, S B College of Science, Kalaburagi 585102, Karnataka, India, Department of Medicinal Chemistry, Jungwon University Goesan 28024, Republic of Korea
Email: sbp7910@gmail.com

Received: 02 May 2021, Revised and Accepted: 24 Jun 2021

ABSTRACT

Coumarone is a chemical compound found in many plants. Coumarone having diverse pharmacological properties popularly known as an antimicrobial, Analgesic anti-inflammatory, Anticancer, Antiviral, anticoagulant, antihypertensive, anticonvulsant, antioxidant, and activities. Coumarone was also observed in all green color veggies, and also in fruits and their seeds, dark coffee, tea leafs, further it is used for herbal remedies due to having less toxicity, very cheaper. The most useful method for the synthesis of Coumarone is from phenol and ethyl acetate and also by using catalyst. In this paper we tried to update the observations of authors towards the biological and medicinal significance of novel the natural and synthetic coumarone derivatives.

Keywords: Coumarone derivatives, Biological and Pharmacological activities

INTRODUCTION

Coumarone consists the huge class of phenolic compounds [1, 2]. Coumarone were initially observed in Tonka bean and having thirty different families [3-9]. Coumarone also observed in some of the oils such as cassia oil [10], cinnamon oil [11-16] etc.

As coumarin having the properties of blood thinning and antitumour properties, so it should not be taken while using anticoagulant. In view of these literature surveys, several natural and synthetic coumarin (2-oxo-2H-chromene) derivatives showed various medicinal and pharmacological activities [17-21]. Coumarins are also widely used as therapeutic agents and malignancies [22, 23].

Medicinal applications

Steffen et al. [24] synthesized hydroxycoumarin derivatives and screened on human tumor cells. Egan and his team [25, 26] was observed cytostatic and cytotoxic nature of nitro substituted hydroxycoumarin. Warfarin, a coumarin analog was more or less cytotoxic against tumor cells [27]. Warfarin was reported to inhibit rat mammary carcinoma.

Akmal and team [28, 29] observed synergistic cytotoxicity activity [30]. Kerr et al. [31-37] synthesized compounds that inhibit the Vitamin K and Kam et al. [38] synthesized various isocoumarin derivatives.
Fig. 6: 7-Amino-4-chloro-3-(3-isothioureidopropoxy) isocoumarin

Smirnova and team reported various coumarone derivatives [39]. Wallin et al. [40] and Hart et al. [40] have studied the synthesis and anticoagulant activity of coumarin derivatives. Yamada [42, 43] and team observed the spasmylyptic activity of several coumarin compounds Aminov and team [44]. Observed spasmylytic and hypotensive activities. Brhamabhatt et al. [45] have synthesized various derivatives. Bhosale et al. [46] have reported the synthesis and antipsychotic activity of new coumarinacetamides.

Fig. 7: Bis[4-hydroxy-2-oxo-2H-chromen-3-yl]-[1H-pyrazol-3-yl]-methane

Irena K et al. [47] synthesised the various coumarin complexes. Recently, Antigoni Kotali et al. [48] observed the antileucemic activity of coumarin benzyloxyzone derivatives.

Fig. 8: 7-Hydroxy-8-acetylcoumarin benzy 1hydrazone

Shingare et al. [49] have reported a new methodology for the synthesis of coumarinophosphorothioates from 7-hydroxy coumarin derivatives using O, O-diethyl phosphorochloridithiate in presence of sodium hydroxide and aliquat 336 as catalyst.

Biological activities

Desai et al. have mentioned ecofriendly microwave synthesis of imidazole derivatives containing coumarin moiety and their antimicrobial activity.

Fig. 9: 3-(1-(Benzof[di]thiazol-2-yl)-2-mercapto-1H-imidazol-4-yl)-2H-benzopyran-2-one

Sandeep et al. [50, 51] observed significant antimicrobial and anti-inflammatory activities.

Fig. 10: 7Methoxy-4-methyl-8-[5-arylisoaxozol-3-yl]-2H-benzopyran-2-one

Rafat M and team [52] observed antifungal and antibacterial activities.

Fig. 11: 8-Methyl-9H-pyreno[1,2-6]pyran-9-one

Fig. 12: 3-Methyl 2H-anthra[1,2-b]pyran-2-one

Novobiocin, Coumermycin and clorobiocin are potent antibiotics.

Fig. 13: R=H, Na

Fig. 14: Cloromycin
Coumarone derivatives showed strong coronary vasodilating activity.

Recently, the synthetic 7-hydroxy coumarone derivative observed as an antianginal drug.

A number of naturally occurring as well as synthetic furocoumarins such as psoralen etc are well known for their dermal photosensitizing, estrogenic, antibacterial, antifungal, antiviral and insecticidal activities. Marked anti-fertility activity of a number of diphenyl furocoumarins is also attributed to a triaryl ethylene pattern.

Various pyrano benzopyrans are known for their biological activities. Some pyrano benzopyran 2,5 diones are well known for their anticoagulant activity, CNS activity and anti-HIV agents.

Other known antioxidants include curcumin found in turmeric and ginger.

The benzofuran (3,2-b) pyridines and tetrahydropyridines have been reported as potential anti-allergic agents and potential antidepressants.

Pyridine-fused coumarins and benzofuran
Following Coumarone derivatives synthesized in our laboratory

Naganna M. Goudaon et al. [53] synthesized and observed antimicrobial activities of a series of some innovative substituted coumarone derivatives.

Sharanabasappa B. Patil et al. [54], synthesized and observed antimicrobial activity of 6-bromo-3,3′-[1-(1H-indol-2-yl)-1-phenyl-1H-pyrazol-4-yl]acryloyl]-2H-chromen-2-ones, 6-bromo-3-(1,2,5,6-tetrahydro-6-[3-(4-aryl)-1-phenyl-1H-pyrazol-4-yl]-2-thioxopyrimidin-4-yl)-2H-chromen-2-ones, 4-(6-bromo-2-oxo-2H-chromen-3-yl)-5,6-dihydro-6-[3-(4-aryl)-1-phenyl-1H-pyrazol-4-yl] pyrimidin-2(1H)-ones and 6-bromo-3-[4,5-dihydro-5-[3-(4-aryl)-1-phenyl-1H].

CONCLUSION

The natural and Synthetic Coumarone derivatives showed potent biological properties. (such as anti-inflammatory, anticoagulant, antitumoral, antiviral, antidiabetic, antihyperglycemic, antioxidant, and antitubercular, antihypertensive, antitumor, and antiparasitic).

FUNDING

Nil

AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

REFERENCES

1. Y Aoyama, T Katayama, M Yamamoto, H Tanaka, K Kon. A new antitumor antibiotic product, demethylch-treisine. Isolation and biological activities. J Antibiotics 1992;45:67–8.

2. M Ibranish, M Askari, A Sahbekar, D Hadjipavlou Litsa. Evaluation of antioxidant, anti-inflammatory and lipoygenase inhibitory activities of the prenylated coumarin umbelliprenin. DARU 2009;17:99–103.

3. WC Evans. Trease and evans pharmacognosy, Elsevier Ltd. 16th edition; 2009.

4. JA Mead, JN Smith, RT Williams. Studies in detoxication. 71. The metabolism of hydroxycoumarins. Biochem J 1958;68:67–74.

5. C Spino, M Dodier, S Sotheeswaran. Anti-HIV coumarins from natural and Synthetic Coumarone derivatives. DARU 2009;17:99–103.

6. S Rosselli, AM Maggio, N Faraone. The cytotoxic properties of natural coumarins isolated from roots of ferula subbostrata and other coumarin-containing plants. J Nat Prod 2009;14:1701–6.

7. Atta-ur-Rahman, M Shabbir, S Ziauddin Sultan, A Jabbar, M Choudhary. Cinnamates and coumarins from the leaves of Murraya paniculata. Phytochemistry 1997;44:683–5.

8. J Cohen. Critical review of the toxicology of coumarin with special reference to interspecies differences in metabolism and hepaticotoxicity and their significance to man. Food Cosmetics Toxicol 1979;17:277–89.

9. RW Fuller, HK Bokesch, KR Gustafson. HIV inhibitory coumarins from latex of the tropical rainforest tree calophyllum teymanii var. inophylloide. Bioorganic Med Chem Lett 1994;4:1961–4.

10. J Choi, KT Lee, H Ka, WT Jang, JH Jung, HJ Park. Constituents of the essential oil of the cinnamonum cassia stem bark and the biological properties. Arch Pharmacal Res 2001;24:418–23.

11. F Bourguad, A Henn, R Larbat. Biosynthesis of coumarins in plants: a major pathway still to be unravelled for cytochrome P450 enzymes. Phytochem Rev 2006;5:293–308.

12. D Bogdal. Coumarins: fast synthesis by Knoevenagel condensation under microwave irradiation. J Chem Res Synposes 1998;8:468–9.

13. BG Lake. Coumarin metabolism, toxicity and carcinogenicity: relevance for human risk assessment. Food Chem Toxicol 1999;37:423–53.

14. D Egan, R O’Kennedy, E Moran, D Cox, E Prosser, RD Thurs. The pharmacology, metabolism, analysis, and applications of coumarin and coumarin-related compounds. Drug Metab Rev 1990;22:503–29.

15. ME Marshall, JL Mohler, K Edmonds. An updated review of the clinical development of coumarin (1,2-benzopyrone) and 7-hydroxycoumarin. J Cancer Res Clin Oncol 1994;120:539–42.

16. RDH Murray. Naturally occurring plant coumarins. In: Progress in the Chemistry of Natural Products, Springer, New York, NY, USA; 1997. p. 2–105.

17. Hudson JB, Towers GHN, Steve M, Doling Peter R. Proc int symp on medicinal plants 1993. Chem Abstr 1996;19:129.

18. Marshall ME, Butler K, Cantrell J, Wiseman C, Mendelsohn L. Treatment of advanced malignant melanoma with coumarin and cimetidine: a pilot study. Cancer Chemother Pharmacol 1989;24:665.

19. Cox D, O’Kennedy R, Thurses R. The rarity of liver toxicity in patients treated with coumarin (1,2-benzopyrone). Human Toxicol 1989;8:501.

20. Steffen US, Weber B, Siegers C. Synthesis of a diverse series of phosphocoumarins with biological activities. Res Comm Mol Pathol Pharmacol 1998;99:193.

21. Cook D, Fitzpatrick B, O’Kennedy R, McCormack T, Egan D. Coumarin: biochemical profile and recent developments: John Wiley and Sons: New York, NY; USA; 1997. p. 311–22.

22. Dongmanti Ashok, Bachi Reddy Vanaja, Mdderar Sarja, B Vijaya Lakshmi. Microwave-assisted synthesis of substituted 4-chloro-3,5-dialyl isoxazole derivatives endowed with growth-supporting and antipaptotropic properties. J Med Chem 2008;51:4796–903.

23. Sardari S, Mori Y, Horita K, Riczli, Genova P, Raleva S, Argirova R. Structure-activity relationships of synthetic coumarins as HIV-1 inhibitors. Bioorg Med Chem 2006. https://doi.org/10.1016/j.bmc.2006.08.274

24. Daniele Baruchello, Michele Rizzi, Giuseppina Grisolia, Marco Eleopra, et al. Novel terphenyls and 3,5-diaryl isoxazole derivatives endowed with growth-supporting and antipaptotropic properties. J Med Chem 2009;8:4745–8.

25. Sardari S, Mori Y, Horita K, Riczli, Genova P, Raleva S, Argirova R. Structure-activity relationships of synthetic coumarins as HIV-1 inhibitors. Bioorg Med Chem 2006. https://doi.org/10.1016/j.bmc.2006.08.274

26. Issa M, Omar MM, Sabrah B A, Mohamed SK. Complexes of coumarins and angular phosphacoumarins with biological activities. Res Commun Mol Pathol Pharmacol 1998;99:193–40.

27. Teotia MP, Rastogi DK, Malik WU. Stereochemical features views-as-is spectral data on some nickel[II] complexes of amino ligands viz. 3′,3′-Di-armino-4,4′-dihydroxy diphenyl sulfone and 8-amino-7-hydroxy-4-methylcoumarin. J Agric Chem Acta 1973;7:339.

28. Issa M, Omar MM, Sabrah B A, Mohamed SK. Complexes of terphenyls and 3,5-diaryl isoxazole derivatives endowed with growth-supporting and antipaptotropic properties. J Med Chem 2008;51:4796–903.

29. Sardari S, Mori Y, Horita K, Riczli, Genova P, Raleva S, Argirova R. Structure-activity relationships of synthetic coumarins as HIV-1 inhibitors. Bioorg Med Chem 2006. https://doi.org/10.1016/j.bmc.2006.08.274

30. Daniele Baruchello, Michele Rizzi, Giuseppina Grisolia, Marco Eleopra, et al. Novel terphenyls and 3,5-diaryl isoxazole derivatives endowed with growth-supporting and antipaptotropic properties. J Med Chem 2008;51:4796–903.

31. Sardari S, Mori Y, Horita K, Riczli, Genova P, Raleva S, Argirova R. Structure-activity relationships of synthetic coumarins as HIV-1 inhibitors. Bioorg Med Chem 2006. https://doi.org/10.1016/j.bmc.2006.08.274

32. Daniele Baruchello, Michele Rizzi, Giuseppina Grisolia, Marco Eleopra, et al. Novel terphenyls and 3,5-diaryl isoxazole derivatives endowed with growth-supporting and antipaptotropic properties. J Med Chem 2008;51:4796–903.
33. Brahambhatt DL, Pandya VP, Patel CN, Patel MA. Synthesis of some 3-(4-styryl-6-aryl-pyridin-2-yl)- and 3-(6-styryl-4-aryl-pyridin-2-yl) coumarins. Indian J Chem 2005;44b:1863.

34. Kotali A, Lafazanis IS, Athanassios Papageorgiou, Eleni Chrysogelou, Theodoros Liaiaris, Zacharias Sinakos. Synthesis, characterization and antileukemic activity of 7-hydroxy-8-acetylcoumarin benzoylhydrazone. Molbank 2008;M574:1-4.

35. DiGiovanni J, Cooper CS, Grover JL (eds). Handbook of experimental pharmacology, New York; 1990;94/11:159-22.

36. Wattenberg JLW, Lam LKT, Fladmoe A V Inhibition of chemical carcinogen-induced neoplasia by coumarins and aangelicalactone. Cancer Res 1979;39:1651-4.

37. Nair RV, Fisher EP, Safe SH, Cortez C, Harvey RG, DiGiovanni J. Novel coumarins as potential anticarcinogenic agents. Carcinogenesis 1991;12:65-9.

38. Kampranis SC, Gormley NA, Tranter R, Orphanides G, Maxwell A. Probing the binding of coumarins and cyclothialdines to DNA gyrase. Biochemistry 1999;38:1967-76.

39. Roe SM, Podromou C, O'Brien R, Ladbury JE, Piper PW, Pearl LH. Structural basis for inhibition of the Hsp90 molecular chaperone by the antitumor antibiotics radicicol and geldanamycin. J Med Chem 1999;42:260-6.

40. Yu XM, Shen G, Neckers L, Blake H, Holzbeierlein J, Cronk B, et al. Hsp90 inhibitors identified from a library of novobiocin analogues. J Am Chem Soc 2005;127:12778-9.

41. Y Jacquot. Synthesis, structure, and estrogenic activity of 4-amino-3-(2-methylbenzyl)coumarins on human breast carcinoma cells. Bioorg Med Chem 2007;15:2269.

42. RB Arora, CN Mathur. Relationship between structure and anticoagulant activity of coumarin derivatives. J Pharmacol 1963;20:29.

43. Lan Xie, Yaouo Takeuchi, I. Mark Cosentino, Ku Huing Lee, Anti-AIDS Agents. Synthesis and structure-activity relationships of (5'R,4'R)-(+)-cis-khellactone derivatives as novel potent anti-HIV agents. J Med Chem 1999;42:2662.

44. Nakagawa Goto K, Nakamura S, Lee KH, Antitumor Agents. Syntheses and evaluation of dietary antioxidant-taxoid conjugates as novel cytotoxic agents. Biorg Med Chem Lett 2007;17:2894.

45. Moon YJ, Wang X, Morris ME. Dietary flavonoids: effects on xenobiotic and carcinogen metabolism. Toxicol In Vitro 2006;20:187–210.

46. Hoult JRS, Pava M. Pharmacological and biochemical actions of simple coumarins: natural products with therapeutic potential. Gen Pharm 1996;27:713.

47. Neichi T, Koshikara Y, Murota SI. Inhibitory effect of esculetin on 5-lipoxygenase and leukotriene biosynthesis. Biochem Biophys Acta 1983;753:130.

48. Fylaktakidou KC, Hadjipavlou Litina D, Litinas KE, Nicolaides DN. Natural and synthetic coumarin derivatives with anti-inflammatory/antioxidant activities. Carr Pharm Design 2004;10:3013.

49. Nicolaides DN, Filaktakidou KC, Litinas KE, Hadjipavlou Litina DJ. Synthesis and biological evaluation of several coumarin-4-carboxamidoxime and 3-coumarin-4-yl-1,2,4-oxadiazole derivatives. Eur J Med Chem 1999;33:715–24.

50. Nicolaide SDN, Fylaktakidou KC, Litinas KE. Hadjipavlou Litina d. J Eur Heterocyclic Chem 1998;35:619.

51. Sumakanth M, Sukanya M, Sruthi K. Antibacterial activity of mannich bases of coumarins. Eur J Biomed Pharm Sci 1999;6:288-94.

52. Naiil Mamata Devendra, Bodke Yadav D, M Vijay Kumar, BC Revanasiidappa. An efficient one-pot synthesis of coumarin-amino acid derivatives as potential anti-inflammatory and anti-tumor agents. Synth Commun 2020;50:1210-6.

53. Parameshwarappa G, Lingamani J, Sharanabasappa B Patil, Naganna M Goudgaon. Synthesis and anti-microbial activity of thiazole substituted coumarins. Heterocycl Commun 2009;15:343-8.

54. Sharanabasappa B Patil, NM Goudgaon. Synthesis and antimicrobial activity of novel coumarone analogues. Int J Pharm Sci Res 2019;10:960-5.