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Natural occurrence and biological activity of various coumarin derivatives

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Abstract

Coumarins are members of the benzopyrones family of compounds. Various coumarin derivatives are biologically active and display pharmaceutical and medicinal properties. Coumarin is a secondary metabolite that is naturally present in a variety of plants as well as essential oils. It is found in relatively high concentrations. Due to the easy availability and biological activity of coumarin derivatives, many chemists have focused their attention on isolating from plants and characterizing and synthesizing coumarin derivatives in the laboratory. The diversity-oriented synthetic routes have resulted in the production of interesting derivatives, such as furanocoumarins, coumarin sulfamates (Coumates) and pyranocoumarins. These derivatives are useful in antitumor, anti-HIV therapy and photo-chemotherapy, as well as stimulants for the central nervous system, anti-bacterials, dyes, anti-inflammatory and anti-coagulants. This review aims to explain the occurrence, biological activities, and characterization of different coumarin derivatives.

Keywords: Natural occurrence, biological activity and chracterisation.

Introduction

Benzopyran-2-one is the nucleus of coumarin derivatives whose nomenclature was established by IUPAC (Vogel, 1820). There have been reports of different biological activities associated with several naturally occurring compounds, including a coumarin moiety. It is to be anticipated that, in a manner analogous to isomeric flavonoids, coumarins might impact the initiation and scavenging of reactive oxygen species (ROS) and influence activities involving free radical-mediated damage. This can be anticipated because it is analogous to something that can happen with isomeric flavonoids. Coumarin has been shown to alleviate tissue swelling and inflammation. In addition, both coumarin and its 7-hydroxy-derivative can suppress the manufacture of prostaglandin, which is a process that requires fatty acid hydroperoxy intermediates.

They are naturally obtained from plants or can be synthesised, and they are polyphenolic chemicals. They exhibit a diverse range of biological activities and behaviours, which supports the idea that they could be used as therapeutic agents for a number of different disorders. The degree of the biological activity appears to be defined by the structural qualities of the molecules, which are associated with their physicochemical properties.

Methodology

Coumarin is a benzopyrone, which is a significant class of benzopyrones (Wu et al., 2001) that is present in nature and functions as a structural subunit of more complex natural compounds (Maier et al., 2000; Zhou et al., 2000).

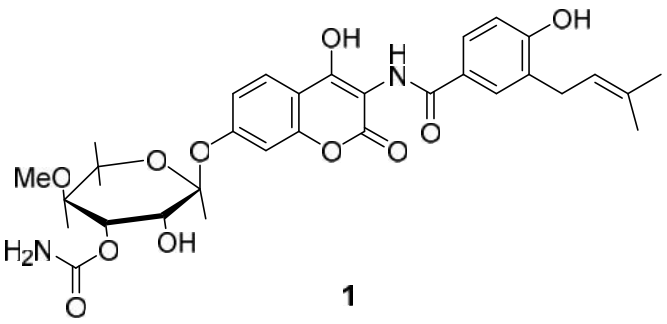

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Figure 1: Novobiocin

The majority of these compounds participate in various biological processes (Gellert et al., 1976; Murray et al., 1982). For instance, Novobiocin **1** (Fig. 1), which may be synthezised from *Streptomyces niveus*, is an antibiotic that is generated from coumarin and functions as a competitive inhibitor of the bacterial ATP binding gyrase B component. This prevents relaxed DNA from being negatively supercoiled (Levine et al., 1998).

The antidote for venomous snake bites is called wedelolactone **2** (Fig. 2), and it is a substance that occurs naturally (Naser et al.,1994). Due to the fact that its triplet excited state frequently occurs in high yield it is also put to use in the production of flash pumpable laser dyes and the photographic industry (Jones et al., 1999; Raboin et al., 2000).

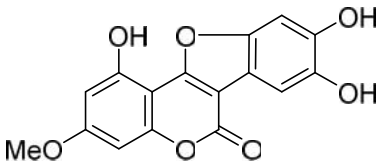

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Figure 2: Wedelolactone

Numerous coumarin derivatives are known to exhibit important photophysical and biological actions (Murakami et al., 2000; Wu et al., 2001). These findings were published in two separate studies. In mouse macrophage RAW 264.7 cells, coumarin compounds osthenol **3** (Fig. 3) isolated from Citrus hystrix DC fruit demonstrated a significant inhibitory activity toward both lipo-polysaccharide (LPS)- and interferon (IFN-induced NO production). Concurrently, a formation relationship investigation found that coumarins that include prenyl unit(s) were classified as a prominent class of NO production inhibitors. This classification was reached as a result of the study's findings (Murakami et al., 1999).

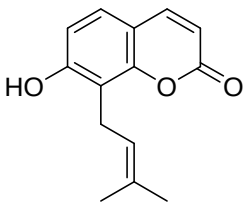

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Figure 3: Osthenol

Prasertcharoensuk et al. (2007) and Prasad et al. (2010) reported the occurrence of nordentatin **4** (Fig. 4), in Clausena plants. Recent research has focused on two analytes of dentatin and nordentatin, the compounds in the coumarin group that show the distinguished activities to protect the neurodegenerative condition (Booyarat et al., 2009). In addition, these two analytes showed the activity of bacterial inhibition (Wu et al., 1982), such as anti-myco bacterial tuberculosis and antifungal (Sunthitikawinsakul et al., 2003).

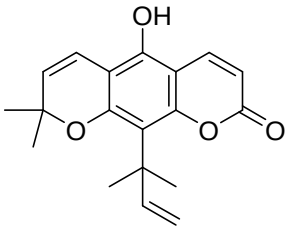

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Figure 4: Nordentatin

The main source of ponfolin **5** (Fig. 5) in *Citrus* plants. Ponfolin (Poncirus trifoliata, Citrus trifoliata) is derived from the root of the Trifoliate Orange (Poncirus trifoliata, Citrus trifoliata (Furukawa, et al., 1986). Ponfolin, a naturally occurring chemical, has been proposed as a disease suppressor by inhibiting NO production.

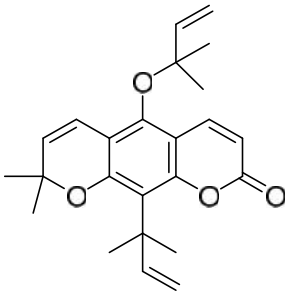

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Figure 5: Ponfolin

Clausenidin **6** (Fig. 6) is a wild shrub that has been used as a folk remedy for snakebite and as a detoxification agent (Wu et al., 1982). Clausenidin is mostly found in the roots of Clausena heptafylla. Clausenidin **6** is produced by treating ponfolin 5 with hydrochloric acid. Because the crude ethanolic extract of this plant had anti-bacterial activities, it was sought to isolate this bioactive component from it.

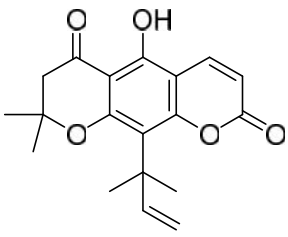

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Figure 6: Clausenidin

Prangenin **7** (Fig. 7) had antimicrobial properties. The MIC value for prangenin against *P. aeruginosa*, *S. aureus*, *S. typhi*, and *S. paratyphi* B was 300 micro g/ml. According to these findings, *Peucedanum zenkeri* seed extract includes anti-bacterial compounds that are effective against *Salmonella* species that cause typhoid and paratyphoid fevers, as well as certain bacterium strains that cause urogenital infections. Prangenin is found in various *Prangos* species, including *P. equisetoides*, *P. hissarica*, *P. ferulaceae*, and *P. fedtschenkoii* (Razavi et al., 2008).

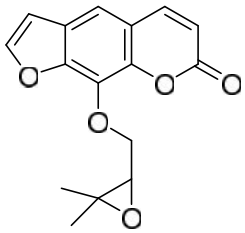

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Figure 7: Prangenin

Micromelum minutum bark is a good source of phebalosin **8** (Fig. 8) (Tantishaiyak et al., 1986). Phebalosin was harmful to brine shrimp and prevented the growth of crown gall tumours on potato discs.

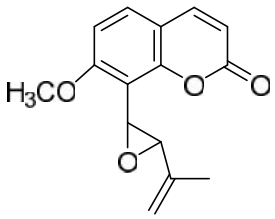

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Figure 8: Phebalosin

Geiparvarin **9** (Fig. 9) was determined to be the most typical of the coumarins tested for anticancer action (Borges et al., 2005). Geiparvarin is a coumarin-based natural compound extracted from the leaves of *Geijera parviflora*.

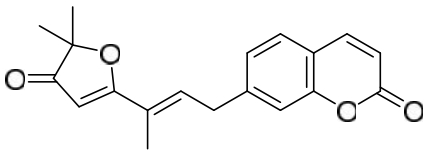

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Figure 9: Geiparvarin

Warfarin **10** (Fig. 10) is considered the most effective coumarin anticoagulant due to its high potency and favourable pharmacokinetics. While the racemicsodium salt is the commercial form, the anti-coagulant activity of the (S)-(-) enantiomer is six times that of the (+) enantiomer.

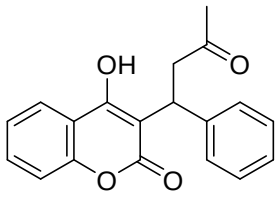

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Figure 10: Warfarin

Others discovered a shortage of vitamin-K ("Koagulations-Vitamin") in experimental animals led to a strong tendency to bleed some years after dicumarol **11** (Fig. 11) was discovered. It was later shown that animals lacking vitamin-K were likewise hyper prothrombinemic. In 1939, the structure of vitamin-K was discovered, and Link quickly discovered that dicumarol and vitamin-K had similar structures. Vitamin-K counteracts the action of dicumarol, which prevents the synthesis of normal levels of prothrombin.

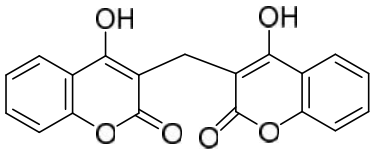

Figure 11: Dicumarol

The precise molecular foundation for these activities has only recently been discovered. Link worked with clinicians at the Wisconsin General Hospital and the Mayo Clinic to investigate dicumarol's capacity to control clotting in human patients after testing it on animals. Dicumarol was finally approved for use in clinical medicine in 1941. Since then, it has been widely used as an anti-coagulant, receiving particular notoriety after treating President Eisenhower following a heart attack in 1955 (Nicole et al., 2005).

Separation and Identification

Several separations and identification techniques have been devised, and they have proven to be very useful in isolating simple coumarins and analogues from plants. Plant components are extracted using appropriate solvents and purified using column chromatography and HPLC. Different spectroscopic techniques characterize all compounds, with UV-VIS, FT-IR, ^{1}H-NMR, ^{13}C-NMR, and MS being the most useful in the field.

Conclusion

In conclusion, most coumarin derivatives are biologically active and show medicinal properties. These biological active coumarin derivatives are easily obtained from different families of plants. These biologically active compounds are purified by chromatographic technique and characterized using different spectroscopic techniques.

Acknowledgments

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References

Booyarat, C., Monthakantitat, O., Srisoi, S., Thongthoom, T., Songsiang, U., & Prasertcharoensuk, W. (2009). Neuroprotective effects of extracted compounds from *Clausenaharmandiana* Linn. Proceeding of the Asian Federation for Pharmaceutical Sciences.Centennial Hall, Kyushu University, Japan.

Borges, F., Roleira, F., Milhazes , N., Santana, L., and Uriarte, E. (2005). Simple Coumarins and

Analogues in Medicinal Chemistry: Occurrence, Synthesis and Biological Activity. *Current Medicinal Chemistry*, 12(8): 887-916.

Gellert, M., O'Dea, M. H., Itoh, T., Tomizawa, J. I. P. (1976). Novobiocin and coumermycin inhibit DNA supercoiling catalyzed by DNA gyrase. *Natl. Acad. Sci. U.S.A.*, 73: 4474-4478.

Furukawa, H., Ju-ichi, M., Kajiura, I., & Hirai, M. (1986). Ponfolin: A New Coumarin from Trifoliate Orange. *Chem.Pharm. Bull*., 34: 3922.

Jones, G., Ann, J., & Jimenez, A. C. (1999). Intramolecular photoinduced electron transfer for cations derived from azole-substituted coumarin dyes. *Tetrahedron Lett*., 40: 8551-8555.

Levine, C., Hiasa, H., & Marians, K. J. (1998). DNA gyrase and topoisomerase IV: biochemical activities, physiological roles during chromosome replication, and drug sensitivities. *Biochim. Biophys. Acta*., 1400: 29-43.

Maier, W., Schmidt, J., Nimtz, M., Wray, V., and Strack, D. (2000). Secondary products in mycorrhizal roots of tobacco and tomato. *Phytochemistry*., 54: 473-479.

Murakami, A., Gao, G., Kim, O.K., Omura, M., Yano, M., Ito, C., Furukawa, H., Jiwajinda, S., Koshimizu, K., and Ohigashi, H. (1999). Identification of Coumarins from the Fruit of *Citrus hystrix* DC as Inhibitors of Nitric Oxide Generation in Mouse Macrophage RAW 264.7 Cells. *J. Agric. Food Chem.*, 47: 333.

Murakami, A., Gao, G., Omura, M., Yano, M., Ito, C., Furukawa, H., Takahasi, D., Koshimizu, K., and Ohigashi, H. (2000). 1, 1-Dimethylallylcoumarins potently suppress both lipopolysaccharide-and interferon-γ-induced nitric oxide generation in mouse macrophage RAW 264.7 cells. *Bioorg. Med. Chem. Lett*., 10: 59.

Murray, R. D. H., Mêndez, J., & Brown, S. A. (1982). The natural coumarines: Occurrence, Chemistry, and Biochemistry, Wiley: New York.

Naser-Hijazi, B., Stolze, B., and Zanker, K. S. (1994). Second proceedings of the International Society of Coumarin Investigators; Springer: Berlin.

Nicole, K., Robert, D. S., and Robert, L. H. (2005). Hemorrhagic Sweet Clover Disease, Dicumarol, and Warfarin: The Work of Karl Paul Link. *The Journal of Biological Chemistry*, 280(08): e6.

Prasad, K. N., Xie, H., Hao, J., Yang, B., Qiu, S., & Wei, X. (2010). Antioxidant and anticancer activities of 8-hydroxypsoralen isolated from ample [*Clausena lansium* (Lour.) Skeels] peel. *Food Chem*., 118: 62-66.

Prasertcharoensuk, W., Boonyarat, C., & Wangboonskul, J. (2007). Study on antioxidative activity from *Clausena harmandiana*. Proceedings of the Fifth Indochina Conference on Pharmaceutical Sciences Pharmacy for Sustainable Development. Siam City Hotel, Bangkok, Thailand.

Raboin, J. C., Beley, M., & Kirsch, G. (2000). Pyridine-fused coumarins: a new class of ligands for ruthenium complexes with enhanced spectral absorption. *Tetrhedron Lett*., 41: 1175-1177.

Razavi, S. M., Nazemiyeh, H., Hajiboland, R., Kumarasamy, Y., Delazar, A., Nahar, L., and Sarker, S. D. (2008). Coumarins from the aerial parts of *Prangos uloptera* (Apiaceae). *Brazilian Journal of Pharmacognosy*, 18 (1): 1-5.

Sunthitikawinsakul, A., Kongkathip, N., Kongkathip, B., Phonnakhu, S., Daly, J. W., & Spande, T. F. (2003). Coumarins and carbazoles from *Clausena excavata* exhibited anti-mycobacterial and antifungal activities. *Planta Med*., 69: 155-157.

Tantishaiyakul, V., Pummangura, S., and Chaichantipwth, C. (1986). Phebalosin from the Bark of *Micromelum minutum*. *Journal of Natural Products*, 49 (1): 180.

Vogel, A. Gilbert´s (1820). The introduction of coumarin. *Am. Phys*., 64: 161.

Wu, J., Liao, Y., and Yang, Z. (2001). Synthesis of 4-Substituted Coumarins via the Palladium-Catalyzed Cross-Couplings of 4-Tosylcoumarins with Terminal Acetylenes and Organozinc Reagents. *J. Org. Chem*., 66: 3642.

Wu, T. S., & Furukawa, H. (1982). Biological and phytochemical investigation of *Clausena excavate*. *Lloydia*. 45: 718-270.

Wu, T. S., Kuoh, C. S., and Furukawa, H. (1982). Acridone alkaloids from *Severinia buxifolia*. *Phytochemistry*, 21: 1771.

Wu, J., Liao, Y., and Yang, Z. (2001). Synthesis of 4-Substituted Coumarins via the Palladium-Catalyzed Cross-Couplings of 4-Tosylcoumarins with Terminal Acetylenes and Organozinc Reagents. J. *Org. Chem*., 66: 3642-3645.

Zhou, P., Takaishi, Y., Duan, H., Chen, B., Honda, G., Itoh, M., Takeda, Y., Kodzhimatov, O. K., and Lee, K. H. (2000). Coumarins and bicoumarin from Ferula sumbul: anti-HIV activity and inhibition of cytokine release. *Phytochemistry*, 53: 689-697.

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