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Coumarins: Paving the Future Path Towards Antibacterial and Anti-inflammatory Therapies

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Abstract: ***Coumarins are a versatile class of benzopyrones whose derivatives, both synthesized and natural have been explored for a wide range of activities like anti-bacterial, anti-viral, anti-fungal, anti-cancer, anti-coagulant, antioxidant, neuroprotective, anti-diabetic and anti-inflammatory activities. Two top classes of therapeutics in growing demand are antibacterials and anti-inflammatory agents. This review focuses on the studies carried out to explore the antibacterial and anti-inflammatory potentials of coumarins, both synthetic and naturally occurring, from 2021 to 2024.***

Keywords: Coumarins, Antibacterial, Anti-inflammatory, Synthesis, Extracts

1. Introduction

Coumarins are a class of aromatic compounds where each member possesses a 2H–1–benzopyran-2-one nucleus. Coumarins come under the benzopyrone family, wherein each of the members possesses a benzene ring fused to an α–pyrone ring. This unique structure is responsible for a vanilla–like odour of many of the coumarins. Coumarins are further classified into simple coumarins, furocoumarins, dihydrofurocoumarins, pyranocoumarins, phenylcoumarins and biscoumarins.

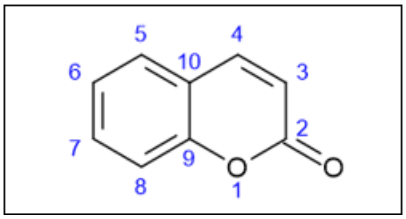

Figure 1: Structure of coumarin nucleus (2H-1–benzopyran-2-one).

The name coumarin is derived from the French word for the tonka bean (*Dipteryx odorata*), "coumarou," since coumarin was first isolated from tonka beans [1],[2]. Coumarins are usually found naturally but are also synthesized to ensure a good yield for the synthesis of useful coumarin derivatives. In the plant kingdom, there are three major sources of coumarins: Apiaceae, Asteraceae and Rutaceae [3]. Coumarins are important leads in drug discovery and development as they possess a plethora of activities, including anti-bacterial, anti-viral, anti-fungal, anti-cancer, anti-coagulant, antioxidant, neuroprotective, anti–diabetic and anti–inflammatory activities. There have also been many derivatives of coumarins and their conjugates studied for various activities as listed above [3],[4].

Today, there is a constant public outcry for more effective and safer therapeutics, particularly antibacterials and anti-inflammatory agents. The main reasons are antibacterial resistance and adverse effects of chronic administration of NSAIDs in people with chronic illnesses [11],[12],[19],[20]. This is where the application of the coumarin ring as a promising scaffold comes into picture. There have been insights into the studies of coumarins and their derivatives for antibacterial and anti-inflammatory activities [5],[6],[7],[8]. Hence, this review touches upon the studies carried out on coumarins in plant extracts as well as designed and synthesized coumarin derivatives spanning from 2021 to 2024, focussing on antibacterial and anti-inflammatory studies and displaying the structures of the best-performing molecules. Hence, this review can intrigue and motivate researchers who are aspiring to work on coumarins and contribute significantly to fruitful drug discovery and development.

2. Materials and methods

The databases of PubMed, Science Direct, and A & V publications were searched for suitable research articles based on antibacterial and anti-inflammatory studies carried out on coumarins. Mostly the articles dating from 2021 to 2024 were chosen and read.

3. Results and Discussion

3.1 Coumarins for Antibacterial Activity

Loganathan et al., (2024) designed and synthesized anthraquinone-coumarin conjugates and evaluated them for biological activities, including *in vitro* antibacterial activity. They found that compound 1t possessed the highest activity against *E. aerogenes* [9].

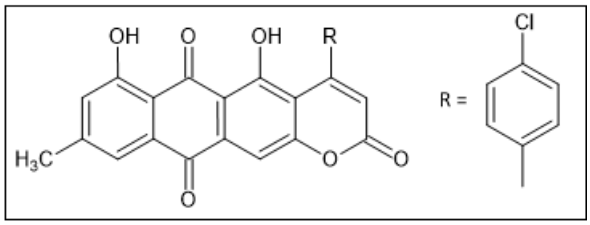

Figure 2: Structure of compound 1t.

Emam et al., (2023) designed and synthesized a series of coumarin derivatives; they were evaluated for antibacterial activity. Compound 3b (figure 2) was found to possess the lowest minimum inhibitor concentration (MIC) and minimum bactericidal concentration (MBC) out of all the compounds (including the standard: novobiocin), against *K. pneumoniae*. It also exhibited high stability in mammalian plasma. Compound 3b also inhibited Gram–negative DNA gyrase, with an IC_{50} lower than that of novobiocin. However, *in silico* studies reveal that novobiocin has a greater binding affinity to the DNA gyrase active site than that of compound 3b [10].

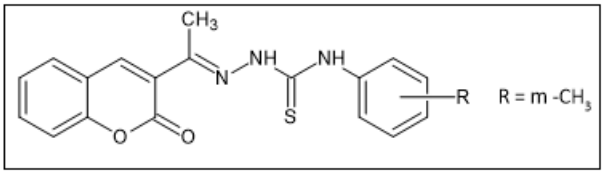

Figure 3: Chemical structure of compound 3b.

Zeng et al., (2023) designed and synthesized a series of piperazine–hybridized coumarin indolylcyanoeneones, and evaluated them for antibacterial activity; out of which, a derivative, 11f, possessed the most promising activity [11].

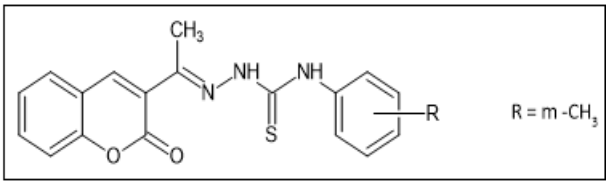

Figure 4: Chemical structure of derivative 11f.

Liu et al., (2023) synthesized a series of coumarin derivatives and evaluated them for activity against *P. aeruginosa, via in vitro* and mechanistic studies and the derivative 4t was found to have the most promising activity. It also enhanced the synergistic action of antibiotics ciprofloxacin and tobramycin by more than 200-1000–fold compared to the single-dose antibiotic treatments, when tested in healthy female wound–afflicted balb/c mice [12].

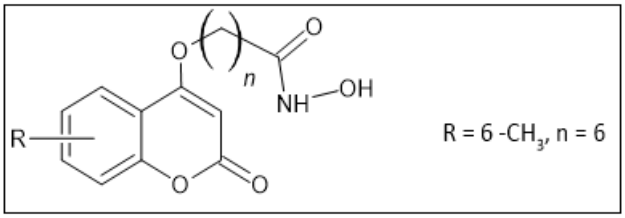

Figure 5: Chemical structure of derivative 4t.

Li et al., (2023) synthesized three series of polysaccharide derivatives tethered with coumarins and evaluated them for biological activity, including antibacterial activity. Compounds 10B and 10C exhibited the highest degree of antibacterial activity [13].

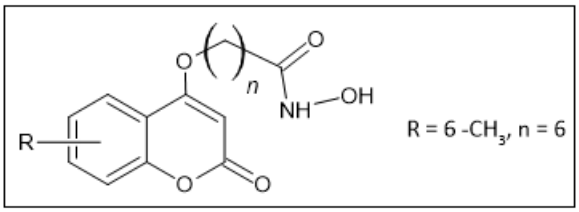

Figure 6: Chemical structures of derivatives: 10B and 10C

Abdelaziz et al., (2023) designed and synthesized a series of novel coumarin–N–heterocyclic hybrids bearing these N–heterocyclic moieties: quinoline, acridine and neocryptolepine. These hybrids were then evaluated for biological activity, which includes antibacterial activity. Results from the antibacterial assay showed that compounds 10b, 13b, 10c and 13c were found to possess the highest antibacterial potential [14].

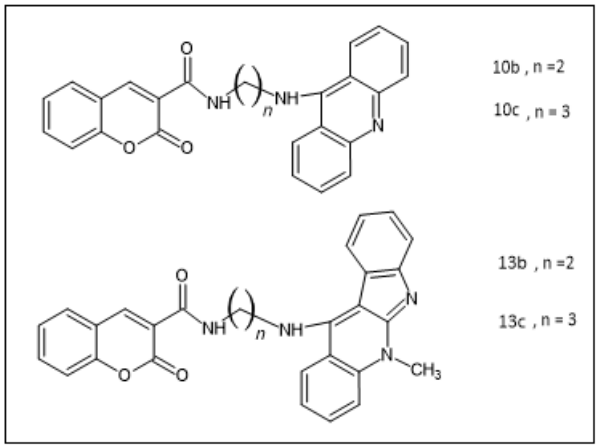

Figure 7: Chemical structures of derivatives: 10b, 10c, 13b, 13c

Zala et al., (2023) designed and synthesized a series of novel piperazine–based cinnamic acid–bearing coumarin derivatives and subjected them to biological activity evaluation, including *in vitro* antibacterial activity and molecular docking. The study concluded that derivatives 7d, 7f, 7g and 7k could be promising leads for developing more effective antimicrobial drug molecules [15].

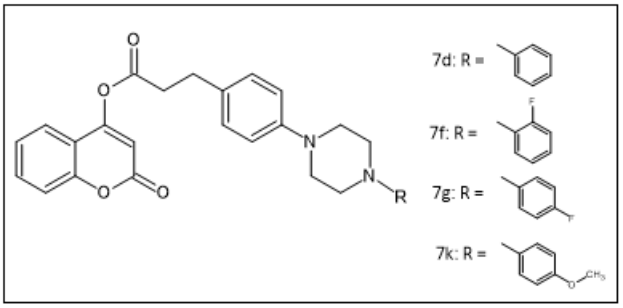

Figure 8: Chemical structures of derivatives: 7d, 7f, 7g and 7k.

Nikitin et al., (2023) carried out the phytochemical profiling of ethanolic extracts of different *Artemesia* L. species and evaluated them for biological activity. Coumarins 7–geranyloxycoumarin, isofraxidin, scoparone and scopoletin were found in varying proportions in all the extracts. The minimum concentration for antibacterial activity of all the extracts was 150 mcg/ml. The *A. dracunculus* cv. Smaragd extract had a selective effect against Gram-positive *R. iranicus* and *B. subtilis, A. scoparia* cv. Tavrida extract possessed selective effect against Gram-negative *A. tumefaciens* and *X. arboricola* bacteria [16].

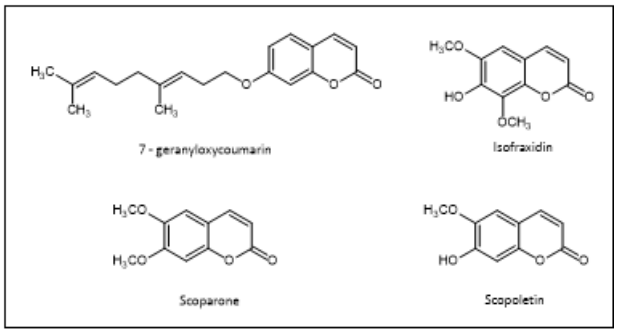

Figure 9: Coumarins present in ethanolic extracts of different *Artemesia* L. species

D et al., (2023) synthesized various coumarin–chalcones and subjected them to *in vitro* biological evaluation of activity. Out of all the hybrids, compounds 3a to 3e showed antibacterial potential [17].

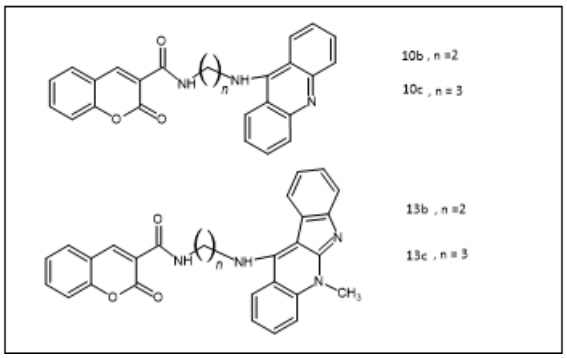

Figure 10: Chemical structures of coumarin–chalcone hybrids 3a – e.

Tajani et al., (2023) subjected some coumarin derivatives to evaluation of anti–quorum sensing and anti–biofilm activity against *Pseudomonas aeruginosa* PAO1 using *in vitro* and *in silico* approach. Overall, results showed that 4–farnesyloxycoumarin and farnesiferol B were the most potential derivatives for anti–quorum sensing and anti–biofilm activity against *Pseudomonas aeruginosa* PAO1 [18].

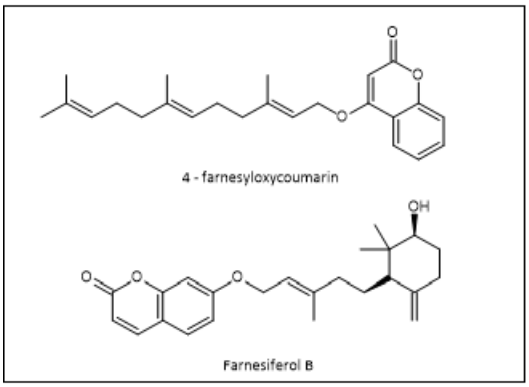

Figure 11: Chemical structures of 4–farnesyloxycoumarin and farnesiferol B.

Koszelewski et al., (2023) synthesized coumarin–α–amino dimethyl phosphonate conjugates and evaluated these for synergistic antimicrobial effect of these two pharmacophores. All these derivatives were found to possess good antibacterial activity. This proved the synergy between coumarin and α–amino dimethyl phosphonate [19].

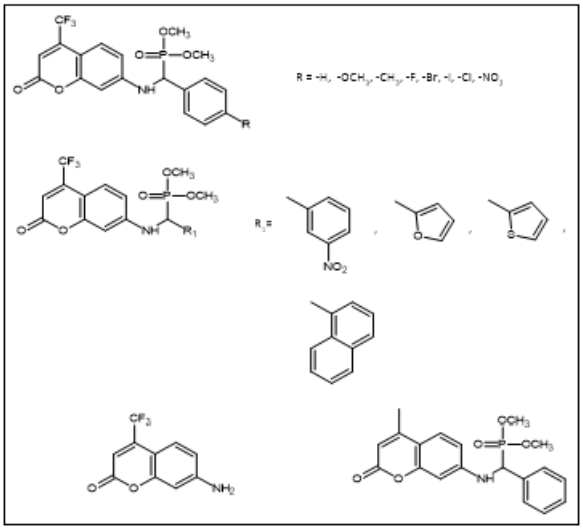

Figure 12: Designed coumarin–α–amino dimethyl phosphonate conjugates and an amino coumarin

Hamid et al., (2023) designed derivatives of 3–substituted coumarins and subjected them to *in vitro* and *in silico* evaluation of inhibitory potential against *E. coli* HsIV. Results reveal that the below pictured derivatives were found to possess the most activity [20].

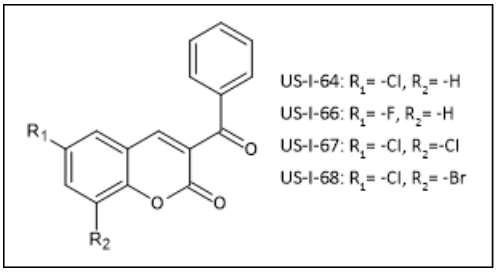

Figure 13: Chemical structures of most promising derivatives of 3–substituted coumarins.

Sasaki et al., (2023) synthesized various derivatives of novobiocin and tested them for antigonococcal activity and

pharmacokinetics. Based on the results, out of the designed derivatives, derivative 47 was found to perform the best [21].

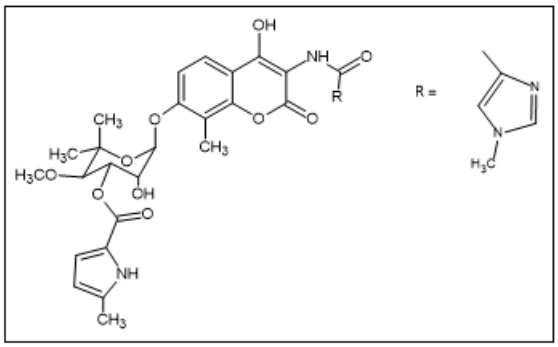

Figure 14: Chemical structure of novobiocin derivative 47.

Reddy et al., (2023) designed and synthesized various coumarin-thymidine analogs and subjected them to evaluation of activity against *Mycobacterium tuberculosis*. For this evaluation, *in vitro* antitubercular assay, molecular docking and toxicity studies were carried out. The results of the study showed that compound 1k was the most active compound which was found to be safe and possess an excellent docking score [22].

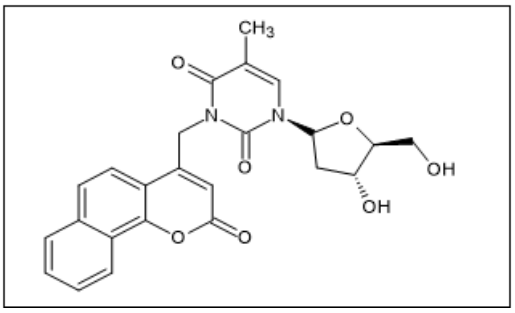

Figure 15: Chemical structure of the most active coumarin-thymidine analog: Compound 1k.

Tang et al., (2023) isolated and characterized two new isocoumarin derivatives: Eleuthemarins A and B; the source of these isocoumarins was the Arctic fungus *Eleutheromyces* sp. CPCC 401592. These compounds were then evaluated for biological activity, including *in vitro* antibacterial activity. The results from the study showed eleuthemarin A to possess weak antibacterial activity [23].

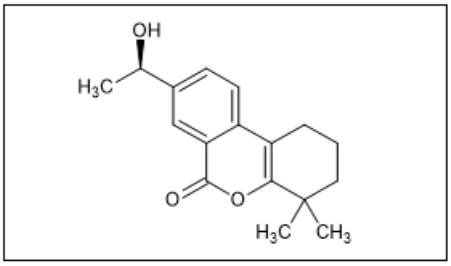

Figure 16: Chemical structure of Eleuthemarin A.

de Sousa et al., (2023) gauged the *in vitro* bactericidal potential of some eugenol–derived coumarins. Out of the coumarins, C1 was found to possess the best activity against *S. aureus* whereas C3 AND C4 possessed the best activity against *E. coli* [24].

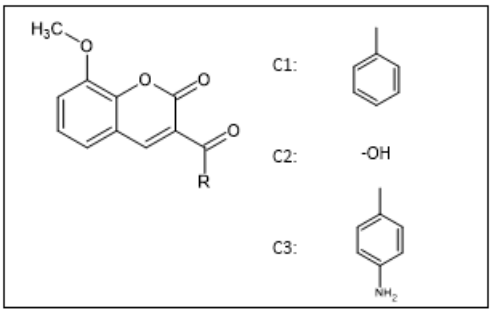

Figure 17: Chemical structures of most active eugenol–derived coumarins.

Sayed et al., (2023) developed new series of thiazoles, pyridines and pyrazoles based on coumarin moiety and evaluated these for antimicrobial potential, including antibacterial potential. The results revealed that compound 12 performed the best in terms of activity against *Bacillus pumilis*; compounds 3, 4 and 12 exhibited remarkable activity against *Streptococcus faecalis*; compound 9 exhibited the best activity against *Enterobacter cloacae*. Most of the designed compounds had good activity against *Escherichia coli* [25].

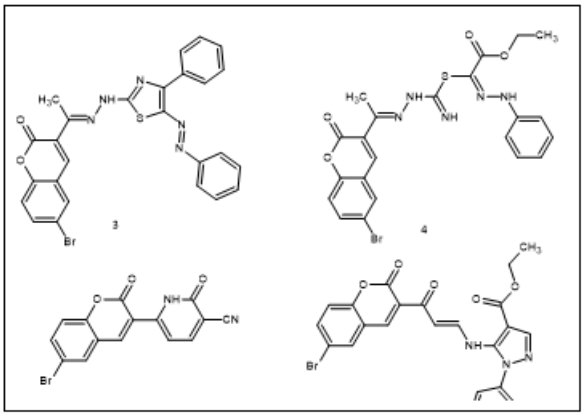

Figure 18: Chemical structures of the most active coumarin derivatives

Araújo-Neto et al., (2023) evaluated the potential of 3–substituted, synthetic coumarins for inhibition of the NorA and MepA efflux pumps of *S. aureus*. This was done by determining *in vitro* MIC, studying the association of coumarins with fluoroquinolones and ethidium bromide (EtBr), assessing the effect on EtBr fluorescence emission, molecular docking, and analyzing the effect on membrane permeability. From the results it is noted that coumarin C1 performed the best [26].

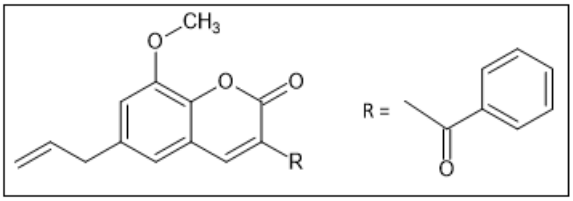

Figure 19: Chemical structure of the best 3–substituted coumarin derivative: coumarin C1.

Pawar et al., (2023) screened diverse families of phytochemicals *in silico* for binding affinity with *N. gonorrhoeae* MurI protein; some compounds were shortlisted and further evaluated for functional, structural, and *in vitro*

antibacterial activity. The results from the study showed that esculetin was found to possess the best activity [27].

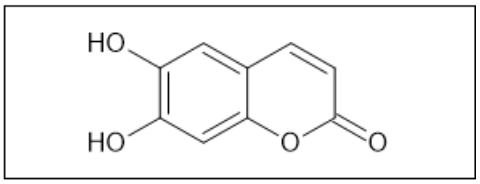

Figure 20: Chemical structure of the most active phytochemical against *N. gonorrhoeae*: Esculetin.

O et al., (2022) synthesized and characterized azo compounds containing 4–methylumbelliferone; these were then evaluated for various biological activities including antibacterial activity. Out of all the azo compounds, 4a, 4b and 4c were found to have the best antitubercular activity, while 4a and 4d possessed the best activity against other bacterial strains [28].

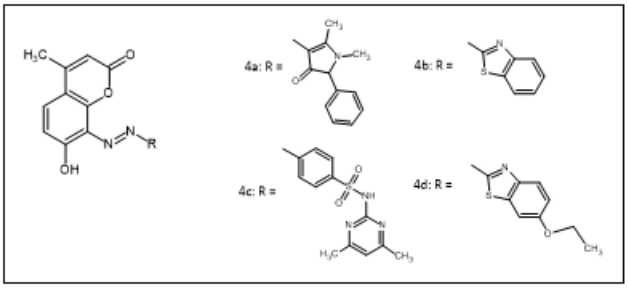

Figure 21: Chemical structures of the most active 4-methylumbelliferone–based azo compounds.

Selim et al., (2022) carried out phytochemical profiling of the methanolic extract of *Pistacia lentiscus* bark and evaluated this extract for biological activity, which includes antibacterial activity. The extract was found to have good antibacterial activity. The phytochemical profile of this extract revealed presence of 2.0 % coumarins. However, the identities of these coumarins have not been determined [29].

Duan et al., (2022) evaluated natural compounds obtained from the TCMSP database for antitubercular activity via molecular docking and *in vitro* assay. The results from the study showed that daphnetin, a coumarin exhibited the best antitubercular activity [30].

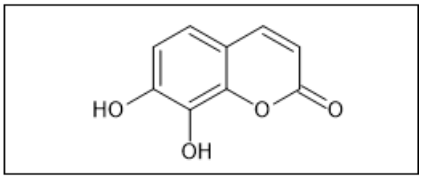

Figure 22: Chemical structure of daphnetin

Xu et al., (2022) designed and evaluated *N*-nitrosoaniline NO donors possessing a 7-amino-4-methylcoumarin scaffold for NO release. They discovered that NO donor 3a, possessed the optimal NO release. They further discovered via *in vitro* and *in vivo* mice studies that 3a, when administered with Levofloxacin (Lev) offered a synergistic effect to eliminate Methicillin-resistant *Staphylococcus aureus* (MRSA) biofilms and heal wounds infected with bacteria [31].

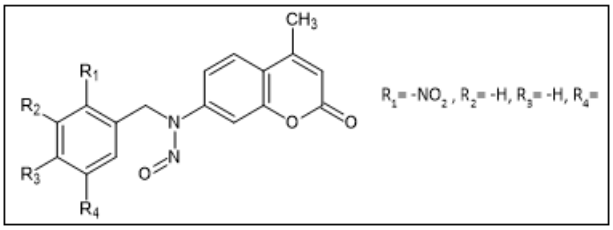

Figure 23: Chemical structure of NO donor 3a.

Vasava et al., (2022) conducted *in silico* screening of proposed benzimidazole derivatives with the protein target, *Mycobacterium tuberculosis* Enoyl Reductase (Inha), to determine the therapeutic potential of these derivatives to treat TB. The results convinced the authors that the proposed derivatives possessed promising anti-TB activity by inhibition of Inha. Three of the derivatives, from 'set 4' possessed a coumarin moiety [32].

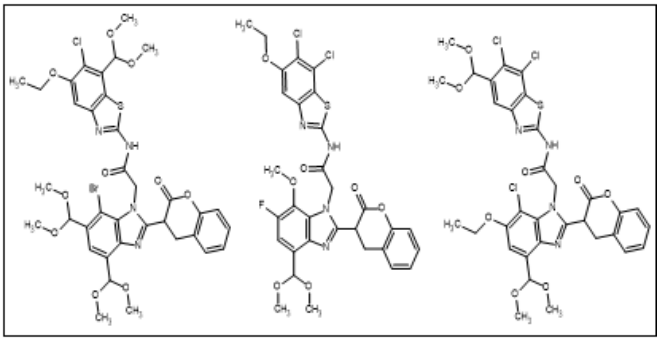

Figure 24: Chemical structures of benzimidazole derivatives with coumarin moiety.

3.1 Coumarins for Anti-inflammatory Activity

Tu et al., (2023) elucidated the detailed mechanism of the neuroprotective action of urolithin A in preventing Alzheimer's disease; this was done by kinase–profiling and the researchers confirmed that dual-specific tyrosine phosphorylation-regulated kinase 1A (DYRK1A) is the main target of urolithin A [33].

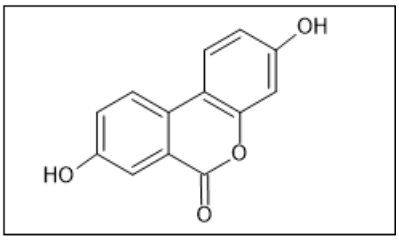

Figure 25: Chemical structure of urolithin A.

Guo et al., 2023 elucidated and confirmed the mechanism of daphnetin (figure 24) in alleviating lipopolysaccharide (LPS)-induced septic lung injury by network pharmacology as well as mice and cell models. The researchers concluded that the inhibition of MAPK/NF-κB/NLRP3 pathway and upregulation of CD38 are caused by daphnetin, leading to the beneficial therapeutic effect [34].

Karabulut Uzunçakmak et al., (2023) explored the effects of suberosin in alleviating sepsis–induced lung injury; this study was performed using male Wistar rat models of cecal ligation and puncture (to induce sepsis in the rats). The study

concluded that suberosin ameliorated sepsis–related lung injury in a dose–dependent fashion [35].

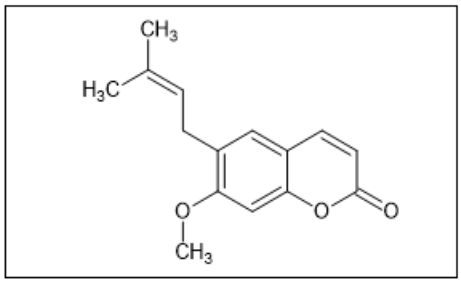

Figure 26: Chemical structure of suberosin

Min et al., (2023) synthesized 23 pyranocoumarin derivatives and evaluated for anti–inflammatory effects on lipopolysaccharide–induced inflammation in RAW264.7 macrophages. Out of the derivatives, coumarin derivative 2 possessed the best anti–inflammatory activity [36].

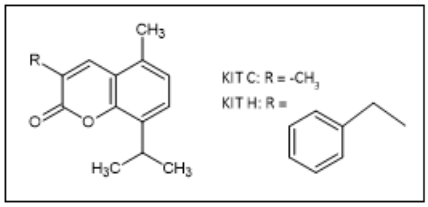

Figure 27: Chemical structure of the most active pyranocoumarin derivative: derivative 2.

Luo et al., (2023) evaluated the therapeutic potential of bergapten in treating combined allergic rhinitis and asthma syndrome (CARAS) by using BALB/c mice with CARAS. The researchers observed that bergapten ameliorated CARAS after PM2.5 exposure, by balancing Treg/Th17 expression and suppressing STAT3 and MAPK activation in the mice [37].

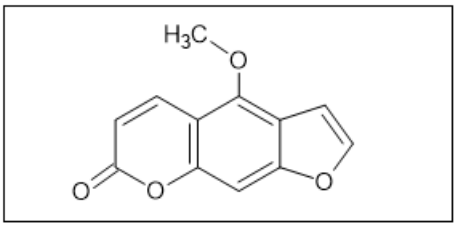

Figure 28: Chemical structure of bergapten.

Ghany et al., (2023) designed, synthesized and conducted anti-inflammatory evaluation of coumarin analogs that incorporated curcumin and other heterocyclic moieties. The evaluation was done using LPS-induced macrophages. Analog 14b performed the best [38].

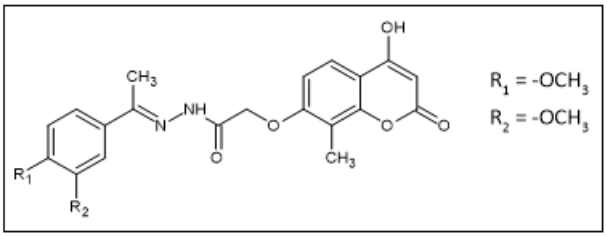

Figure 29: Chemical structure of coumarin analog 14b.

Choo et al., (2023) synthesized minutuminolate, 7 methoxy-8-(2-acetoxy-3-methyl-1-oxobut-2-enyl) coumarin and muralatin I and evaluated them for anti-inflammatory activity against tumor necrosis factor-alpha (TNF-α) production in lipopolysaccharides-stimulated RAW264.7 cells. Muralatin I showed potent TNF-α inhibition [39].

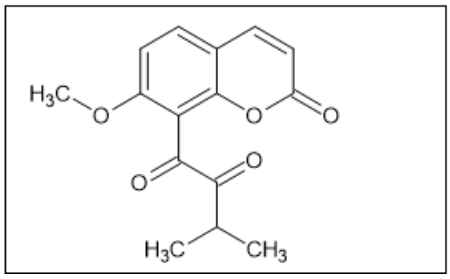

Figure 30: Chemical structure of Muralatin I.

Jiang et al., (2023) explored the targets and mechanisms of osthole in alleviating rheumatoid arthritis. Results from network pharmacology and molecular docking suggested that the anti-inflammatory action of osthole contributed to its activity against rheumatoid arthritis and that AMP-activated protein kinase (AMPK) was the potential target of osthole. *In vitro* studies using TNF-α induced FLS cells revealed that osthole inhibited the secretion of inflammatory factors of RA fibroblast-like synoviocytes (FLS), which the researchers attributed to the activation of AMPK by osthole to inhibit the activation of NLRP3 inflammasome; they also observed that AMPK-induced activation lead to generation of mitochondria; this in turn lead to occurrence of apoptosis and the decrease of ROS in FLS. Results from *in vivo* studies using CIA rat models testified the anti-RA potential of osthole [40].

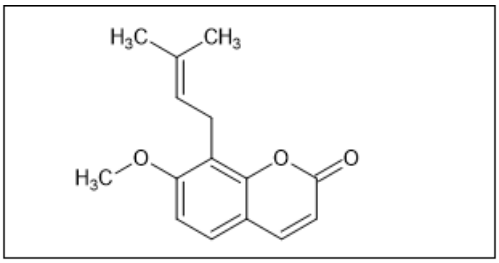

Figure 31: Chemical structure of osthole

Kumar et al., (2023) synthesized 19 3-substituted analogs of scoparone and performed *in vitro and in vivo* screening for anti-inflammatory activity using various methods. The results from the studies led to the conclusion that the scoparone analog 3 possessed the greatest anti-inflammatory potential [41].

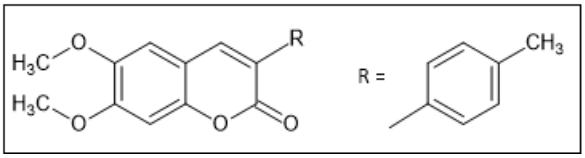

Figure 32: Chemical structure of scoparone analog 3.

Liliana Porras-Dávila et al., (2023) evaluated dichloromethane fractions of the leaves of *Distictis buccinatoria* containing select constituents including the coumarins daphnoretin and herniarin for biological activity. The isolated fractions of daphnoretin and herniarin were evaluated for anti-inflammatory activity using 12-O-tetradecanoylphor bol-13-acetate-induced auricular edema in

mice. The inhibition of local edema by herniarin fraction was found to be 86.92% and for daphnoretin, 86.41%. The fractions containg daphnoretin and herniarin reduced the concentrations of IL-1β, TNF-α, and IL-6, while also increasing the production of IL-10. Hence the authors concluded that daphnoretin and herniarin possess promising anti-inflammatory activity [42].

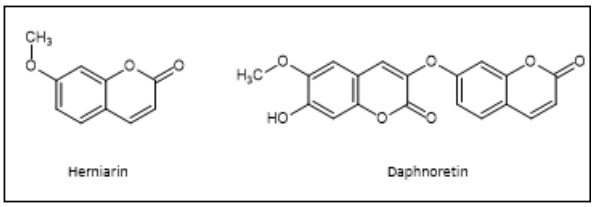

Figure 33: Chemical structures of herniarin and daphnoretin.

S. J. Hamid & Salih, (2022) designed and synthesized four Schiff bases of 7-hydroxy-4-formyl coumarin and 7-methoxy-4-formyl coumarin; these were subjected to *in silico* and *in vitro* evaluation of anti-inflammatory action. *In silico* evaluation was done by molecular docking and determination of druglikeliness *via* Lipinski's rule of five. *In vitro* evaluation was done by the protein denaturation assay. Schiff base 7 was found to have the best overall results [43].

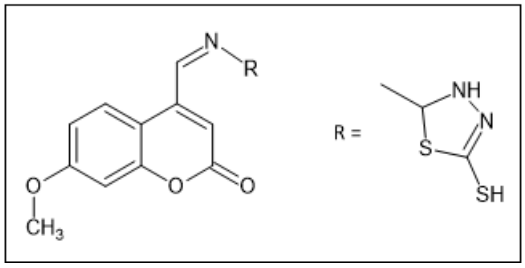

Figure 34: Chemical structure of Schiff base 7.

Apweiler et al., (2022) evaluated the anti-neuroinflammatory effects of two coumarin compounds: KIT C and KIT H in human neuroblastoma cells and primary murine microglia. Both compounds showed varying effects for pro- and anti-inflammatory parameters [44].

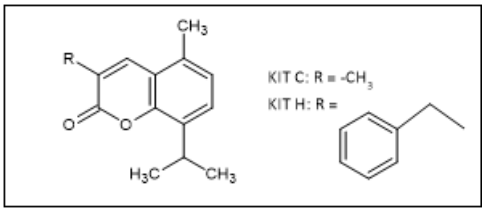

Figure 35: Chemical structures of coumarin-based compounds evaluated for anti-neuroinflammatory effects.

Mosebarger et al., (2022) performed an *in silico* evaluation of osthole derivatives for anti-inflammatory potential. Molecular docking was done for the targets: NF-κB, TNF-α, and ERK1. The derivatives were also evaluated for drug potential. Based on the overall results, protonated demethoxy osthole 1 showed the best potential [45].

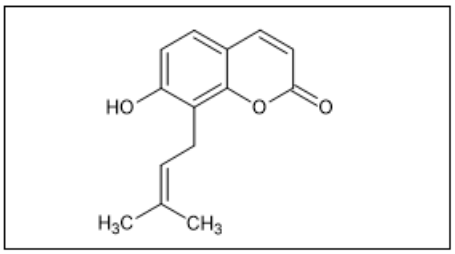

Figure 36: Chemical structure of the most active derivative: protonated demethoxy osthole 1.

Faheem et al., (2022) explored the anti-neuroinflammatory potential of natural compounds, including bergapten (figure 31) in rat models of paclitaxel-associated neuroinflammatory pain. The results showed that all the natural compounds tested has potent anti-neuroinflammatory action [46].

Jahan et al., (2022) prepared the methanolic extract of *Chukrasia velutina* bark and subjected the extract through various *in vitro*, *in vivo* and *in silico* assays to determine what type of biological activities the extract possesses. The phytoconstituents present in the extract were also determined. The results from the study suggested that 5,7-dimethoxycoumarin and scopoletin (figure 9) possessed the most promising activity, especially in terms of analgesic and antipyretic actions [47].

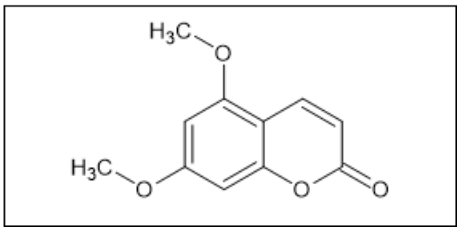

Figure 37: Chemical structure of 5,7-dimthoxycoumarin

It is observed that there are some similarities in the structures of all the coumarins studied: presence of methoxy and hydroxy groups, halogens especially chloro, fluorine, bromine and methyl groups. These groups were mostly aromatic groups attached to the coumarin nuclei. Additionally, among the coumarins studied for antibacterial activities, presence of nitro group, heterocycles like piperazine, oxygen, nitrogen and sulphur-containing five-membered heterocycles were more common than those studied for anti-inflammatory activities. Presence of methoxy group is the most common and seen in coumarins studied for both antibacterial and anti-inflammatory studies.

4. Conclusions

Coumarins that incorporate aromatic and non-aromatic methoxy, hydroxy, chloro, fluorine, bromine and methyl groups can be designed for the evaluation of both antibacterial and anti-inflammatory activities. Additionally, aromatic nitro group, heterocycles like piperazine, oxygen, nitrogen and sulphur-containing five-membered heterocycles can also be considered for incorporation in coumarins undergoing antibacterial evaluation.

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References

[1] Murray, R.D, The naturally occurring coumarins, Prog. Chem. Org. Nat. Prod, 83, pp. 1-619, 2002.
[2] Sarker, S.D., Nahar, L., Chemistry for Pharmacy Students: General, Organic and Natural Product Chemistry, John Wiley & Sons Ltd., Chichester, pp. 363-364, 2007.
[3] Sree, B. K., Preethi, J. P., & Kumar, P. K., "Synthesis, Characterization and Biological Activity of Coumarin Derivatives", Research J. Science and Tech, 4(6), pp. 252–257, 2012.
[4] Fotopoulos, I., & Hadjipavlou-Litina, D., "Hybrids of Coumarin Derivatives as Potent and Multifunctional Bioactive Agents: A Review. Medicinal Chemistry (Shariqah (United Arab Emirates))", 16(3), pp. 272–306, 2020.
[5] G, A. C., Gondru, R., Li, Y., & Banothu, J., "Coumarin-benzimidazole hybrids: A review of developments in medicinal chemistry", European Journal of Medicinal Chemistry, 227, 2022.
[6] Mujeeb, S., Singh, K., Yogi, B., Ansari, V., & Sinha, S., "A Review on Coumarin Derivatives as Potent Anti-tuberculosis Agents", Mini Reviews in Medicinal Chemistry, 22(7), pp. 1064–1080, 2022.
[7] Patil, S. A., Kandathil, V., Sobha, A., Somappa, S. B., Feldman, M. R., Bugarin, A., & Patil, S. A., "Comprehensive Review on Medicinal Applications of Coumarin-Derived Imine-Metal Complexes", Molecules (Basel, Switzerland), 27(16), 2022.
[8] Kumar, S., Arora, A., Kumar, R., Senapati, N. N., & Singh, B. K., "Recent advances in synthesis of sugar and nucleoside coumarin conjugates and their biological impact",Carbohydrate Research, 530, pp. 1-13, 2023.
[9] Loganathan, V., Ahamed, A., Radhakrishnan, S., Z. Gaafar, A. R., Gurusamy, R., & Akbar, I., "Synthesis of anthraquinone-connected coumarin derivatives via grindstone method and their evaluation of antibacterial, antioxidant, tyrosinase inhibitory activities with molecular docking, and DFT calculation studies", Heliyon, 10(3), e25168, pp.1-15, 2024.
[10] Emam, S. H., Hassan, R. A., Osman, E. O., Hamed, M. I. A., Abdou, A. M., Kandil, M. M., Elbaz, E. M., & Mikhail, D. S., "Coumarin derivatives with potential anticancer and antibacterial activity: Design, synthesis, VEGFR-2 and DNA gyrase inhibition, and in silico studies", Drug Development Research, 84(3), pp. 433–457, 2023.
[11] Zeng, C., Avula, S. R., Meng, J., & Zhou, C., "Synthesis and Biological Evaluation of Piperazine Hybridized Coumarin Indolylcyanoenones with Antibacterial Potential", Molecules (Basel, Switzerland), 28(6), pp. 1-29, 2023.
[12] Liu, J., Zhao, S. Y., Hu, J. Y., Chen, Q. X., Jiao, S. M., Xiao, H. C., Zhang, Q., Xu, J., Zhao, J. F., Zhou, H. B., Zheng, J. X., & Sun, P. H., "Novel Coumarin Derivatives Inhibit the Quorum Sensing System and Iron Homeostasis as Antibacterial Synergists against Pseudomonas aeruginosa", Journal of Medicinal Chemistry, 66(21), pp. 14735–14754, 2023.
[13] Li, Q., Yang, Y., Li, Y., Mi, Y., Ma, X., Jiang, A., & Guo, Z., "Enhanced biological activities of coumarin-functionalized polysaccharide derivatives: Chemical modification and activity assessment" International Journal of Biological Macromolecules, 253(Pt 2), pp. 1-16, 2023.
[14] Abdelaziz, E., El-Deeb, N. M., Zayed, M. F., Hasanein, A. M., El Sayed, I. E.-T., Elmongy, E. I., & Kamoun, E. A., "Synthesis and in-vitro anti-proliferative with antimicrobial activity of new coumarin containing heterocycles hybrids", Scientific Reports, 13(1), 22791, pp. 1-12, 2023.
[15] Zala, A. R., Rajani, D. P., & Kumari, P., "Synthesis, molecular docking, ADME study, and antimicrobial potency of piperazine based cinnamic acid bearing coumarin moieties as a DNA gyrase inhibitor", Journal of Biochemical and Molecular Toxicology, 37(1), 2023.
[16] Nikitin, E., Fitsev, I., Egorova, A., Logvinenko, L., Terenzhev, D., Bekmuratova, F., Rakhmaeva, A., Shumatbaev, G., Gatiyatullina, A., Shevchuk, O., & Kalinnikova, T., "Five Different Artemisia L. Species Ethanol Extracts' Phytochemical Composition and Their Antimicrobial and Nematocide Activity", International Journal of Molecular Sciences, 24(18), pp. 1-25, 2023.
[17] D, B., N, A., YE, M., WS, K., & N, H., "Synthesis and pharmacological properties of coumarin-chalcones", MethodsX, 11, 102488, pp. 1-12, 2023.
[18] Tajani, A. S., Tehranizadeh, Z. A., Pourmohammad, A., Pourmohammad, A., Iranshahy, M., Farhadi, F., Soheili, V., & Fazly Bazzaz, B. S., "Anti-quorum sensing and antibiofilm activity of coumarin derivatives against Pseudomonas aeruginosa PAO1: Insights from in vitro and in silico studies", Iranian Journal of Basic Medical Sciences, 26(4), pp. 445–452, 2023.
[19] Kowalczyk, P., Koszelewski, D., Brodzka, A., Kramkowski, K., & Ostaszewski, R., "Evaluation of Antibacterial Activity against Nosocomial Pathogens of an Enzymatically Derived α-Aminophosphonates Possessing Coumarin Scaffold", International Journal of Molecular Sciences, 24(19), pp. 1-13, 2023.
[20] Hamid, M., Salar, U., Rashid, Y., Azim, M. K., Khan, K. M., Naz, S., Aziz, T., Alharbi, M., Alshammari, A., & Alasmari, A. F., "Determining the 3-substituted Coumarins inhibitory potential against the HslV protease of E. coli", European Review for Medical and Pharmacological Sciences, 27(19), pp. 9169–9182, 2023.
[21] Sasaki, K., Takada, H., Hayashi, C., Ohya, K., Yamaguchi, Y., Takahashi, Y., Igarashi, M., & Shibasaki, M., "Synthesis of novobiocin derivatives and evaluation of their antigonococcal activity and pharmacokinetics", Bioorganic & Medicinal Chemistry, 92, 2023.
[22] Reddy, D. S., Sinha, A., Kurjogi, M. M., Shanavaz, H., & Kumar, A., "Design, synthesis, molecular docking, and biological evaluation of coumarin-thymidine analogs as potent anti-TB agents", Archiv Der Pharmazie, 356(5), pp. 134-147, 2023.
[23] Tang, Y., Hu, J., Guo, Z., Bai, J., Du, Q., Zhang, T., Dai, S., Yu, L., & Zhang, D., "Eleuthemarins A and B, two new isocoumarin derivatives from the Arctic fungus Eleutheromyces sp. CPCC 401592", The Journal of Antibiotics, 76(12), 2023.

[24] de Sousa, A. K., Rocha, J. E., de Freitas, T. S., Freitas, P. R., Pereira, R. L. S., Júnior, F. N. P., Brancaglion, G. A., de Paulo, D. C., Carvalho, D. T., de Menezes, I. R. A., dos Santos, F. A. V., Coutinho, H. D. M., & Júnior, L. J. Q., "Photobiological effect of eugenol-derived 3-benzoylcoumarin associated with led lights against MDR microorganisms", Fundamental & Clinical Pharmacology, 37(2), pp. 316–323, 2023.

[25] Sayed, Mariam & Elsharabasy, Salwa & Abdelaziem, Anhar, "Synthesis and antimicrobial activity of new series of thiazoles, pyridines and pyrazoles based on coumarin moiety", Scientific Reports, 13(1), pp. 1-13, 2023.

[26] Araújo-Neto, J. B. de, Oliveira-Tintino, C. D. de M., de Araújo, G. A., Alves, D. S., Ribeiro, F. R., Brancaglion, G. A., Carvalho, D. T., Lima, C. M. G., Mohammed Ali, H. S. H., Rather, I. A., Wani, M. Y., Emran, T. B., Coutinho, H. D. M., Balbino, V. de Q., & Tintino, S. R., "3-Substituted Coumarins Inhibit NorA and MepA Efflux Pumps of Staphylococcus aureus", Antibiotics (Basel, Switzerland), 12(12), pp. 1-14, 2023.

[27] Pawar, A., Konwar, C., Jha, P., Kant, R., Chopra, M., Chaudhry, U., & Saluja, D., "Bactericidal activity of esculetin is associated with impaired cell wall synthesis by targeting glutamate racemase of Neisseria gonorrhoeae", Molecular Diversity., pp. 1-16, 2023.

[28] O, N., Bodke, Y. D., B, T., Venkatesh, T., & B, M., "Synthesis, characterization and biological evaluation of heterocyclic compounds containing 4-methylumbelliferone", Journal of Molecular Structure, 1269, 133759, 2022.

[29] Selim, S., Almuhayawi, M. S., Alharbi, M. T., Jaouni, S. K. A., Alharthi, A., Abdel-Wahab, B. A., Ibrahim, M. A. R., Alsuhaibani, A. M., Warrad, M., & Rashed, K., "Insights into the Antimicrobial, Antioxidant, Anti-SARS-CoV-2 and Cytotoxic Activities of Pistacia lentiscus Bark and Phytochemical Profile; In Silico and In Vitro Study", Antioxidants (Basel, Switzerland), 11(5), 2022.

[30] Duan, C., Jiang, Q., Jiang, X., Zeng, H., Wu, Q., Yu, Y., & Yang, X., "Discovery of a Novel Inhibitor Structure of Mycobacterium tuberculosis Isocitrate Lyase", Molecules (Basel, Switzerland), 27(8), 2022.

[31] Xu, Y., Li, H., Xu, S., Liu, X., Lin, J., Chen, H., & Yuan, Z., "Light-Triggered Fluorescence Self-Reporting Nitric Oxide Release from Coumarin Analogues for Accelerating Wound Healing and Synergistic Antimicrobial Applications", Journal of Medicinal Chemistry, 65(1), pp. 424–435, 2022.

[32] Vasava, M., Thacker, S., Jethwa, D., Acharya, P., Bhavsar, Z., & Patel, H., "Identification of novel anti-tuberculosis agent: An in silico investigation", The Indian Journal of Tuberculosis, 69(4), pp. 503–522, 2022.

[33] Tu, H. J., Su, C. J., Peng, C. S., Lin, T. E., Fu, W. C. H., Hsu, K. C., Hwang, T. L., & Pan, S. L., "Urolithin A exhibits a neuroprotective effect against Alzheimer's disease by inhibiting DYRK1A activity", Journal of Food and Drug Analysis, 31(2), pp. 358–370, 2023.

[34] Guo, Y., Zhang, H., Lv, Z., Du, Y., Li, D., Fang, H., You, J., Yu, L., & Li, R., "Up-regulated CD38 by daphnetin alleviates lipopolysaccharide-induced lung injury via inhibiting MAPK/NF-κB/NLRP3 pathway", Cell Communication and Signaling : CCS, 21(1), pp. 1-24, 2023.

[35] Karabulut Uzunçakmak, S., Halıcı, Z., Karakaya, S., Kutlu, Z., Sağlam, Y. S., Bolat, İ., Aydın, P., & Kılıç, C. S., "Suberosin Alleviates Sepsis-Induced Lung Injury in A Rat Model of Cecal Ligation and Puncture", Journal of Investigative Surgery : The Official Journal of the Academy of Surgical Research, 36(1), pp. 1–9, 2023.

[36] Min, S. J., Lee, H., Shin, M. S., & Lee, J. W., "Synthesis and Biological Properties of Pyranocoumarin Derivatives as Potent Anti-Inflammatory Agents", International Journal of Molecular Sciences, 24(12), 2023.

[37] Luo, T., Jia, X., Feng, W. di, Wang, J. yong, Xie, F., Kong, L. dong, Wang, X. jiao, Lian, R., Liu, X., Chu, Y. jie, Wang, Y., & Xu, A. long., "Bergapten inhibits NLRP3 inflammasome activation and pyroptosis via promoting mitophagy", Acta Pharmacologica Sinica, 44(9), pp. 1867–1878, 2023.

[38] Ghany, L. M. A. A., Beshay, B. Y., Youssef Moustafa, A. M., Maghrabi, A. H. A., Ali, E. H. K., Saleem, R. M., Zaki, I., & Ryad, N., "Design, synthesis, anti-inflammatory evaluation, and molecular modelling of new coumarin-based analogs combined curcumin and other heterocycles as potential TNF-α production inhibitors via upregulating Nrf2/HO-1, downregulating AKT/mTOR signalling pathways and downregulating NF-κB in LPS induced macrophages", Journal of Enzyme Inhibition and Medicinal Chemistry, 38(1), pp. 1-13, 2023.

[39] Choo, M. Z. Y., Khaw, L. W. T., & Chai, C. L. L., "Syntheses of Minutuminolate and Related Coumarin Natural Products and Evaluation of Their TNF-α Inhibitory Activities", ACS Omega, 8(44), pp. 41785–41791, 2023.

[40] Jiang, X., Lu, Z., Zhang, Q., Yu, J., Han, D., Liu, J., Li, P., & Li, F., Osthole: A potential AMPK agonist that inhibits NLRP3 inflammasome activation by regulating mitochondrial homeostasis for combating rheumatoid arthritis. Phytomedicine : International Journal of Phytotherapy and Phytopharmacology, 110, 2023.

[41] Kumar, C., Chibber, P., Painuli, R., Haq, S. A., Vishwakarma, R. A., Singh, G., Satti, N. K., & Phatake, R. S., "Scoparone chemical modification into semi-synthetic analogues featuring 3-substitution for their anti-inflammatory activity", Molecular Diversity, 7(3), 2023.

[42] Liliana Porras-Dávila, S., Zamilpa, A., Jiménez-Ferrer, E., Jiménez-Aparicio, A., Alejandra Santillan-Urquiza, M., Díaz-Patricio, F., & Herrera-Ruiz, M., "Anti-Inflammatory and Neuroprotective Effects of Standardized Fractions in Herniarin and Daphnoretin from Distictis buccinatoria", Chemistry & Biodiversity, 20(5), pp. 1-14, 2023.

[43] Hamid, S. J., & Salih, T., "Design, Synthesis, and Anti-Inflammatory Activity of Some Coumarin Schiff Base Derivatives: In silico and in vitro Study", Drug Design, Development and Therapy, 16, pp. 2275–2288, 2022.

[44] Apweiler, M., Streyczek, J., Saliba, S. W., Collado, J. A., Hurrle, T., Gräßle, S., Muñoz, E., Normann, C., Hellwig, S., Bräse, S., & Fiebich, B. L., "Functional Selectivity of Coumarin Derivates Acting via GPR55 in Neuroinflammation", International Journal of Molecular Sciences, 23(2), pp. 1-13, 2022.

[45] Mosebarger, A., Reddi, R. N., Menon, R., & Kammala, A. K., "Computational Screening of the Natural Product Osthole and Its Derivates for Anti-Inflammatory Activity", Life (Basel, Switzerland), 12(4), pp. 1-14, 2022.
[46] Faheem, M., Khan, A. U., Saleem, M. W., Shah, F. A., Ali, F., Khan, A. W., & Li, S., "Neuroprotective Effect of Natural Compounds in Paclitaxel-Induced Chronic Inflammatory Pain", Molecules (Basel, Switzerland), 27(15), pp. 1-15, 2022.
[47] Jahan, I., Sakib, S. A., Alam, N., Majumder, M., Sharmin, S., & Reza, A. S. M. A., "Pharmacological insights into Chukrasia velutina bark: Experimental and computer-aided approaches", Animal Models and Experimental Medicine, 5(4), pp. 377–388, 2022.

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Shreya Shet is set to graduate with a Master's degree in Pharmacy, specializing in Pharmaceutical Chemistry at M.S. Ramaiah University of Applied Sciences, Bengaluru, Karnataka, India. Throughout her academic career, she has always been intrigued by the fascinating world of organic chemistry, especially heterocyclic compounds. A determined research scholar, she is currently studying coumarin derivatives to discover novel antibacterial and anti-inflammatory therapeutics, under the guidance of Dr. Suma B.V an Associate Professor of the same institution. Therefore, she strongly believes that she can make a significant contribution to drug discovery and development and consequently safeguard the health of the public.

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