In vitro antischistosomal activity of 2-aroyl-benzofuran derivatives against *Schistosoma mansoni*

Tatiana M. Vieira [1], Herbert J. Dias [1,2], Daiane A. dos Santos [3], Lizandra G. Magalhães [3], Antônio E. M. Crotti [1*]

[1] *Departamento de Química, Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto, Universidade de São Paulo, 14040-901, Ribeirão Preto – SP, Brazil*
[2] *Instituto Federal de Educação, Ciência e Tecnologia Goiano - Campus Urutaí, 75790-000 Urutaí – GO, Brasil*
[3] *Núcleo de Pesquisas em Ciências Exatas e Tecnológicas, Universidade de Franca, 14404-600, Franca – SP, Brazil*

** Corresponding author. E-mail: millercrotti@ffclrp.usp.br*

ABSTRACT. Five 2-aroylbenzofurans were synthesized by condensation between α-bromoacetone and an *ortho*-hydroxybenzaldehyde or *ortho*-hydroxy-acetophenone and evaluated for their *in vitro* antischistomal effects against adult *Schistosoma mansoni* worms. Below 200 µg/mL, none of the tested 2-aroylbenzofurans killed adult *S. mansoni* worms. On the other hand, at 200 µg/mL all the tested compounds reduced the motor activity of adult *S. mansoni* worms after treatment for 72 h. At 200 µg/mL, compound **1** was the only one to decrease the motor activity of 67% of the worms after incubation for 24 h. The methyl group at C6 and the nature of the substituent at ring A play important roles in the efficacy of 2-aroylbenzofurans in reducing the worm motor activity.

Key words: antischistosomal agents; aroyl-benzofuran; benzofuran; neglected tropical disease; *Schistosoma mansoni*.

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INTRODUCTION

Neglected tropical diseases (NTDs) comprise a group of biologically unrelated tropical diseases that have a disproportionate effect on low-income populations in developing regions of Africa, Asia, and the Americas (Ochola et al., 2021). Although the definition of NTDs can vary, these diseases affect marginalized populations or populations for which treatment options are inadequate or vaccines are poorly available. Occasionally, the affected populations cannot easily access treatments for an NTD, such as schistosomiasis (Ochola et al., 2021). Schistosomiasis, a disease caused by trematode flatworms of the genus *Schistosoma*, is one of the most significant NTDs worldwide. Notwithstanding the significant advances in treating and preventing this disease, it remains markedly widespread, has high morbidity rates, and affects over 240 million people globally (Ally et al., 2024). It is currently estimated that 700 million people are at risk of contracting the disease (Wang et al., 2020). Praziquantel (PZQ) has played a key role in the implementation of population-based disease control programs and in the treatment of schistosomiasis, but it has limited efficacy against juvenile schistosomes (Nawaratna et al., 2020). Moreover, there are numerous reports of strains that are less susceptible to PZQ and of the reduced efficacy of this drug (Summers et al., 2022; Kuevi et al., 2023; Xu et al., 2023)

Aroyl benzofurans and their derivatives have significant potential in drug development. They are particularly useful for their broad range of biological effects, including analgesic (Rádl et al., 2000), antifungal (Gündogdu-Karaburun et al., 2006; Rangaswamy et al., 2012), antibacterial (Coskun et al., 2011; Rangaswamy et al., 2012; Vasconcelos et al., 2014), antileishmanial (Getti et al., 2006), antioxidant (Rangaswamy et al., 2012), anti-HIV (Rida et al., 2006), antitumor (Hayakawa et al., 2004), anti-inflammatory (Yu et al., 2021), antiproliferative, and cytotoxic action (Mahboobi et al., 2007). Several natural and synthetic 2-aroyl benzofurans have gained attention in recent years (Gong et al., 2020; Jin et al., 2020; Panday et al., 2020). Furthermore, some 2-aroyl-benzofuran derivatives can be used as sensors and semiconductors (Oter et al., 2007; Khatua et al., 2020) and as probes for β-amyloid plaques in Alzheimer's disease (Ono Saji, 2015).

As part of our ongoing project on the antiparasitic activity of benzofuran and benzofuran compounds (Dias et al., 2018; Pagotti et al., 2023) and based on previous reports on the antiparasitic activity of 2-aroyl-benzofurans (Moolman et al., 2021), we have investigated the *in vitro* antischistosomal effects of five synthetic 2-aroyl-benzofurans against adult *Schistosoma mansoni* worms.

MATERIAL AND METHODS

Compounds **1–5** were synthesized by carrying out a condensation reaction between 2-bromoacetophenone and an *ortho*-hydroxyaldehyde (Scheme 1) following a previously reported procedure (Yang et al., 2011). Briefly, 2-bromoacetophenone (1.08 g, 5.4 mmol) was added to a 100-mL two-neck round bottom and dissolved in DMF (10 mL). Next, potassium carbonate (2.15 g, 15.6 mmol) was added. After 10 min, an *ortho*-hydroxyaldehyde (**I**, **II**, or **III**) or an *ortho*-hydroxyacetone (**IV** or **V**) was added (Table 2). The reaction was kept under N_2 atmosphere and magnetic stirring at 120 °C and monitored by TLC. After 1-3 h, the reaction mixture was allowed to reach room temperature; next, water (30 mL) was added, and the reaction mixture was stirred for 5 min. The reaction mixtures were vacuum-filtered and dried under reduced pressure, to afford compounds **1–5** in yields ranging between 52 and 70% (Table 2).

Table 2. Quantities of aldehydes and ketones used in the synthesis of compounds **1–5** and the corresponding yields.

Aldehyde or ketone	mmol	Reaction time (h)	Compound (yield)
I	6.0	3	**1** (55%)
II	6.0	1.5	**2** (66%)
III	6.0	2	**3** (59%)
IV	6.0	1	**4** (70%)
V	6.0	3	**5** (52%)

Compounds **1–5** were identified on the basis of their IR, NMR, and MS data and by comparison with literature data (Dias et al., 2017). The corresponding spectral data are listed in Supporting Information.

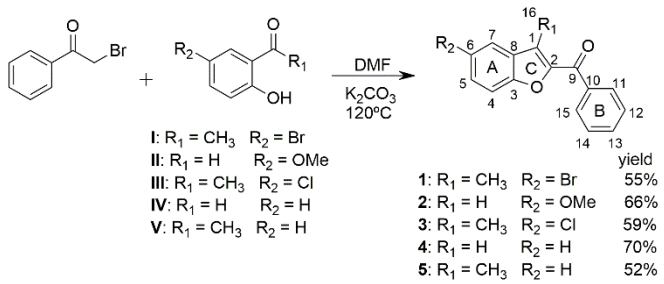
The *S. mansoni* LE (Luiz Evangelista) strain was maintained by transmission through *Biomphalaria glabrata* snails and Balb/c mice. Adult *S. mansoni* worms, both male and female, were recovered after eight weeks from mice infected with 200 cercariae; aseptic methods were used to perfuse the livers and mesenteric veins (Paula et al., 2022). The worms were washed in RPMI 1640 medium (Inlab Diagnonostica, São Paulo, BR) and kept at pH 7.5 with 20 mM HEPES (4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid) supplemented with 100 UI/mL penicillin, 100 g/mL streptomycin, and 10% fetal bovine serum (FBS; Cultilab, Campinas, BRA).

For the *in vitro* tests with *S. mansoni*, one of the tested compounds was dissolved in DMSO (Sigma–Aldrich) and used at concentrations ranging from 12.5 to 200 μg/mL. To this end, one of the tested compounds at a certain concentration was added to the medium containing two adult worms after the worms had adapted to the culture medium for 24 h. The parasites were kept for 120 h and monitored for mortality and alterations in motor activity every 24 h (Manneck et al., 2010). Alteration in the motor activity was classified as either decreased or minimal.

Decreased motor activity was defined as reduced movement compared to the negative control; minimal motor activity was defined as total absence of movement or minimal movement for 2 min (Manneck et al., 2010). After observation (120 h), the culture medium was removed, fresh culture medium without the assayed compound was added, and motility was re-examined for up to 24 h. Parasites in RPMI 1640 medium with 0.1% DMSO or in 1.6 μM (0.48 μg/mL) praziquantel (PZQ, purity ≥ 98%, Sigma–Aldrich Co., S. Louis, MO, USA) were used as the negative and positive control groups, respectively. All the experiments were carried out in quadruplicate and repeated at least three times.

RESULTS AND DISCUSSION

The procedure that was used to synthesize 2-aroyl-benzofurans **1–5** (Scheme 1) afforded the compounds in only one synthesis step in yields that varied from satisfactory to good. The reaction times for the synthesis of compounds **2** and **4**, which derive from aromatic aldehydes, were lower as compared with those of benzofurans **1**, **3**, and **5**, which are derived from aromatic methylketones. This can be explained on the basis of the higher reactivity of aromatic aldehydes compared to aromatic methylketones. The methodology was simple, the reaction time was relatively short, and the reaction was performed under mild conditions. Moreover, the compounds were isolated by vacuum filtration without the need for further chromatographic separation steps. These synthetic advantages make this methodology attractive to obtain these compounds for biological and pharmacological assays.



Scheme 1. Synthesis of compounds **1-5**.

Table 1 lists the *in vitro* antischistosomal effects of 2-aroyl-benzofurans **1–5** against adult *S. mansoni* worms after treatment for 24, 48, or 72 h. At 12.5, 25, and 50 µg/mL, none of the compounds affected the worm motor activity significantly (data not shown). On the other hand, all the worms incubated with compounds **1–5** at 200 µg/mL displayed decreased motor activity after treatment for 72 h. In addition, at this same concentration, compounds **1**, **2,** and **5** reduced the motor activity of all the worms after treatment for 48 h, whereas compound **1** decreased the motor activity in 67% of the worms after incubation for 24 h.

Several biological activities have been reported for 2-aroylbenzofurans **1–5**. For example, compound **3** displays antifungal activity against *C. albicans* (MIC = 25 µg/mL) and *C. glabrata* (MIC = 12.5 µg/mL) (Gündoğdu-Karaburun et al., 2006). Compound **4** is active against HIV (Lambert et al., 2013), whereas compound **5** weakly inhibits DPPH and ABTS radicals (Rangaswamy et al., 2014). However, data on the antiparasitic activity of 2-aroyl-benzofurans are scarce (Moolman et al., 2021). Additionally, no study on the antischistosomal activity of these compounds has been reported.

Dias et al. synthesized the benzofuran neolignan **7** from the dihydrobenzofuran neolignan **6** (Fig. 1) and investigated their *in vitro* schistosomicidal activity against adult *S. mansoni* worms (Dias et al., 2018). At 200 µM, neolignan **6** killed 50% of the treated worms after 72 h, whereas the benzofuran neolignan **7** at 200 µM did not kill any worms after 72 h. These results suggest that neolignans bearing a benzofuran ring are less active than the corresponding dihydrobenzofuran derivatives. Here, compounds **1–5** at concentrations below 200 µg/mL did not affect adult *S. mansoni* worm mortality, which reinforces the previous findings reported by Dias and co-workers and suggests that the benzofuran moiety may not be as important for the antischistosomal activity as the dihydrobenzofuran ring.

Although at 200 µg/mL none of the compounds affected adult *S. mansoni* worm mortality, at the same concentration all the compounds reduced the motor activity after treatment for 72 h. However, their effects on the motor activity differed slightly after 24 and 48 h probably due to the small structural differences of compounds **1–5**. For example, a comparison between the results obtained for compounds **4** and **5** indicates that the methyl group at C1 may boost the motor activity after 24 and 48 h. On the other hand, the higher activity of compound **2** (an H at C1 and an OCH_3 at C6) compared to compound **3** (a CH_3 at C1 and a Cl at C6) suggests that the nature and the position of the substituents at ring A also plays an essential role in the effects of 2-aroylbenzofurans **1–5** on the motor activity. The presence of a methoxy group in the structure of compound **2** is likely responsible for its increased activity compared to compound **4,** whereas a Cl at C6 decreases the bioactivity of compound **3** compared to compound **5.** The role played by the aromatic methoxy and chlorine groups on the antiparasitic activity of curcuminoids has been addressed by Souza and co-workers (Souza et al., 2021). The authors reported that adding electron-releasing groups increases the anti-*Trypanosoma cruzi* activity, whereas incorporating an electron-withdrawing chlorine substituent in the aromatic rings of monoketone curcuminoids lowers or completely abolishes the anti-*T. cruzi* activity (Souza et al., 2021). Nevertheless, the presence of a Br at C6 boosts the antischistosomal activity of compound **1** compared to compound **5**. Although bromine is an electron-withdrawing group like chlorine, the former is bulkier than the latter. Therefore, differences between the effects of compounds **3** and **5** may have a steric origin. These results indicate that the effects of these benzofuran compounds on the adult *Schistosoma mansoni* motor activity are potentialized by the presence of a methyl group at C1, and an electron-releasing methoxy group or a bulky bromine atom at C6.

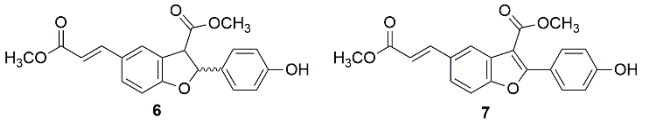


Figure 1. Chemical structures of dihydrobenzofuran neolignan **6** and benzofuran neolignan **7** reported by Dias et al. (Dias et al., 2018).

The reduced mobility of *Schistosoma mansoni* worms can be interpreted as an indication of compromised viability and neuromuscular integrity of the parasite. This reduction in locomotor activity may reflect the direct action of the compound tested on molecular targets involved in the motor control of the worm, which may impair its ability to migrate, mate, and evade the host's immune response. In addition, worms with reduced mobility tend to have a lower capacity for feeding, mating, and oviposition, which contributes to the interruption of the parasite's life cycle and, consequently, to the reduction of the parasite load in the host (Doenhoff et al., 2008).

Table 1. *In vitro* antischistosomal effects of compounds **1–5** on *Schistosoma mansoni*.

Concentration	Time of incubation (h)	Dead worms (%)	Motor activity	
			Decreased	Minimal
0.1%DMSO[a]	24	0±0	0±0	0±0
	48	0±0	0±0	0±0
	72	0±0	0±0	0±0
1 (200 µg/mL)	24	0±0	67±0	0±0
	48	0±0	100±0	0±0
	72	0±0	100±0	0±0
2 (200 µg/mL)	24	0±0	50±0	0±0
	48	0±0	100±0	0±0
	72	0±0	100±0	0±0
3 (200 µg/mL)	24	0±0	0±0	0±0
	48	0±0	0±0	0±0
	72	0±0	100±0	0±0
4 (200 µg/mL)	24	0±0	0±0	0±0
	48	0±0	0±0	0±0
	72	0±0	100±0	0±0
5 (200 µg/mL)	24	0±0	50±0	0±0
	48	0±0	100±0	0±0
	72	0±0	100±0	0±0
PZQ[b] (1.6 µM or 0.48 µg/mL)				

[a] Negative control; [b] Positive control; PZQ: praziquantel

CONCLUSION

Below 200 µg/mL, none of the compounds tested in this study killed adult *S. mansoni* worms. On the other hand, all the tested compounds at 200 µg/mL reduced the motor activity of adult *S. mansoni* worms after treatment for 72 h. The methyl group at C6 and the nature of the substituent at ring A play important roles in the efficacy of the compound in decreasing worm motor activity. This is the first study on the antischistosomal activity of 2-aroylbenzofurans. To obtain a more detailed idea of the structure-activity relationship for 2-aroyl-benzofurans, various compounds containing other substituents at rings A and B should be investigated.

SUPPORTING INFORMATION

Supplementary information (IR, ^{1}H and ^{13}C NMR, and ESI-MS/MS spectra and the results of the antischistosomal assays with compounds **1-5** at concentrations of 12.5, 25, 50, and 100 µg/mL) is available with the article through the journal website.

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AUTHOR CONTRIBUTIONS

TMV and HJD synthesized and identified the compounds; DAS and LGM ran the antischistosomal assays; AEMC worked on the conception, and discussion of results, and drafted the manuscript. All authors agree with the submission of the manuscript and declare that they have not submitted it to another journal during the review process.

REFERENCES

Ally, O., Kanoi, B. N., Ochola, L., Nyanjom, S. G., Shiluli, C., Misinzo, G. and Gitaka, J. (2024). Schistosomiasis diagnosis: Challenges and opportunities for elimination. PLoS Negl Trop Dis, 18, e0012282. https://www.doi.org/10.1371/journal.pntd.0012282.

Coskun, D., Ahmedzade, M. and Kirbag, S. (2011). 3-(Substituted Aryl)-1-benzofuranyl-2-propenones: Antimicrobial properties of some chalcones-type compounds and their 2-pyrazoline derivatives. E-J. Chem., 8, 1574-1581. https://www.doi.org/10.1155/2011/806854.

Dias, H. J., Patrocínio, A. B., Pagotti, M. C., Fukui, M. J., Rodrigues, V., Magalhães, L. G. and Crotti, A. E. M. (2018). Schistosomicidal activity of dihydrobenzofuran neolignans. Chem. Biodiv., 15, e1800134. https://www.doi.org/10.1002/cbdv.201800134.

Dias, H. J., Vieira, T. M., Crevelin, E. J., Donate, P. M., Vessecchi, R. and Crotti, A. E. M. (2017). Fragmentation of 2-aroylbenzofuran derivatives by electrospray ionization tandem mass spectrometry. J. Mass Spectrom., 52, 809-816. https://www.doi.org/10.1002/jms.4024.

Doenhoff, M. J., Cioli, D. and Utzinger, J. (2008). Praziquantel: mechanisms of action, resistance and new derivatives for schistosomiasis. Curr. Opin. Infect. Dis., 21, 659-667. https://www.doi.org/10.1097/QCO.0b013e328318978f.

Getti, G. T., Aslam, S. N., Humber, D. P., Stevenson, P. C. and Cheke, R. A. (2006). The effect of cicerfuran, an arylbenzofuran from *Cicer bijugum*, and related benzofurans and stilbenes on *Leishmania aethiopica*, *L. tropica* and *L. major*. Planta Med., 72, 907-911. https://www.doi.org/10.1055/s-2006-947187

Gong, J., Hu, K., Shao, Y., Li, R., Zhang, Y., Hu, M. and Chen, J. (2020). Tandem addition/cyclization for synthesis of 2-aroyl benzofurans and 2-aroyl indoles by carbopalladation of nitriles. Org. Biomol. Chem., 18, 488-494. https://www.doi.org/10.1039/C9OB02408E.

Gündogdu-Karaburun, N., Benkli, K., Tunali, Y., Uçucu, Ü. and Demirayak, S. (2006). Synthesis and antifungal activities of some aryl [3-(imidazol-1-yl/triazol-1-ylmethyl) benzofuran-2-yl] ketoximes. Eur J Med Chem, 41, 651-656. https://www.doi.org/10.1016/j.ejmech.2005.12.013.

Hayakawa, I., Shiyoa, R., Agatsuma, T., Furukawa, H. and Sugano, Y. (2004). Thienopyridine and benzofuran derivatives as potent anti-tumor agents possessing different structure-activity relationships Bioorg. Med. Chem. Lett., 14, 3411-3414. https://www.doi.org/10.1016/j.bmcl.2004.04.079.

Jin, L.-P., Xie, Q., Huang, E.-F., Wang, L., Zhang, B.-Q., Hu, J.-S., Wan, D. C.-C., Jin, Z. and Hu, C. (2020). Design, synthesis, and biological activity of a novel series of benzofuran derivatives against oestrogen receptor-dependent breast cancer cell lines. Bioorg. Chem., 95, 103566. https://www.doi.org/https://doi.org/10.1016/j.bioorg.2020.103566.

Khatua, R., Sahoo, S. R., Sharma, S. and Sahu, S. (2020). Anisotropic charge transport and optoelectronic properties of wide band gap organic semiconductors based on biphenyl derivatives: A computational study. Synth Met, 267, 116474. https://www.doi.org/10.1016/j.synthmet.2020.116474.

Kuevi, D. N. O., Acquah, F. A., Amuquandoh, A. and Abbey, A. P. (2023). Challenges and proven recommendations of praziquantel formulation. J Clin Pharm Ther, 2023, 3976392. https://www.doi.org/https://doi.org/10.1155/2023/3976392

Lambert, A. A., Azzi, A., Lin, S.-X., Allaire, G., St-Gelais, K. P., Tremblay, M. J. and Gilbert, C. (2013). Dendritic cell immunoreceptor is a new target for antiAIDS drug development: identification of DCIR/HIV-1 inhibitors. PLoS One, 8, e67873. https://www.doi.org/10.1371/journal.pone.0067873.

Mahboobi, S., Sellmer, A., Höcher, H., Garhammer, C., Pongratz, H., Maier, T., Ciossek, T. and Beckers, T. (2007). 2-Aroylindoles and 2-aroylbenzofurans with *N*-hydroxyacrylamide substructures as a novel series of rationally designed histone deacetylase Inhibitors. J. Med. Chem., 50, 4405-4418. https://www.doi.org/10.1021/jm0703136.

Manneck, T., HaggenmÜLler, Y. and Keiser, J. (2010). Morphological effects and tegumental alterations induced by mefloquine on schistosomula and adult flukes of *Schistosoma mansoni*. Parasitology, 137, 85-98. https://www.doi.org/10.1017/S0031182009990965.

Moolman, C., van der Sluis, R., Beteck, R. M. and Legoabe, L. J. (2021). Exploration of benzofuran-based compounds as potent and selective *Plasmodium falciparum* glycogen synthase kinase-3 (PfGSK-3) inhibitors. Bioorg. Chem., 112, 104839. https://www.doi.org/10.1016/j.bioorg.2021.10483.

Nawaratna, S. S. K., McManus, D. P., Gasser, R. B., Brindley, P. J., Boyle, G. M., Rivera, V., Ranasinghe, S. L., Jones, M. K., You, H. and Gobert, G. N. (2020). Use of kinase inhibitors against schistosomes to improve and broaden praziquantel efficacy. Parasitology, 147, 1488-1498. https://www.doi.org/10.1017/S0031182020001250.

Ochola, E. A., Karanja, D. M. S. and Elliott, S. J. (2021). The impact of Neglected Tropical Diseases (NTDs) on health and wellbeing in sub-Saharan Africa (SSA): A case study of Kenya. PLoS Negl. Trop. Dis., 15, e0009131. https://www.doi.org/10.1371/journal.pntd.0009131.

Ono, M. and Saji, H. (2015). Recent advances in molecular imaging probes for β-amyloid plaques. Med. Chem. Comm., 6, 391-402. https://www.doi.org/10.1039/C4MD00365A.

Oter, O., Ertekin, K., Kirilmis, C., Koca, M. and Ahmedzade, M. (2007). Characterization of a newly synthesized fluorescent benzofuran derivative and usage as a selective fiber optic sensor for Fe(III). Sens. Actuators B Chem. , 122, 450-456. https://www.doi.org/1k0.1016/j.snb.2006.06.010.

Pagotti, M. C., Dias, H. J., Candido, A., Oliveira, T. A. S., Borges, A., Oliveira, N. D., Lopes, C. D., Orenha, R. P., Parreira, R. L. T., Crotti, A. E. M. and Magalhaes, L. G. (2023). Exploring synthetic dihydrobenzofuran and benzofuran neolignans as antiprotozoal agents against *Trypanosoma cruzi*. Pharmaceutics, 15, 754. https://www.doi.org/10.3390/pharmaceutics15030754.

Panday, A. K., Ali, D. and Choudhury, L. H. (2020). Cs_2CO_3-mediated rapid room-temperature synthesis of 3-amino-2-aroyl benzofurans and their copper-catalyzed *N*-arylation reactions. ACS Omega, 5, 3646-3660. https://www.doi.org/10.1021/acsomega.9b04169.

Paula, L. A., Santos, M. F. C., Pagotti, M. C., Veneziani, R. C. S., Bastos, J. K., Caffrey, C. R., Ambrósio, S. R. and Magalhães, L. G. (2022). Brazilian green propolis reduces worm burden and hepatic granuloma formation in a *Schistosoma mansoni* experimental murine model. Parasitol Res, 121, 775-780. https://www.doi.org/10.1007/s00436-021-07408-0.

Rádl, S., Hezký, P., Urbánková, J., Váchal, P. and Krejci, I. (2000). Synthesis and analgesic activity of some 1-benzofurans, 1-benzothiophenes and indoles. Collect. Czech. Chem. Comm., 65, 280-296.

Rangaswamy, J., Kumar, H. V., Harini, S. T. and Naik, N. (2012). Synthesis of benzofuran based 1,3,5-substituted pyrazole derivatives: As a new class of potent antioxidants and antimicrobials-A novel accost to amend biocompatibility. Bioorg. Med. Chem. Lett., 22, 4773-4777. https://www.doi.org/10.1016/j.bmcl.2012.05.061c.

Rangaswamy, J., Kumar, H. V., Harini, S. T. and Naika, N. (2014). An easy access to benzofurans via DBU induced condensation reaction of active 2-hydroxy acetophenones with phenacyl chlorides: a novel class of antioxidant agents. J. Heteroc. Chem., 52, 938-943. https://www.doi.org/10.1002/jhet.1971.

Rida, S. M., El-Hawash, S. A. M., Fahmy, H. T. Y., Hazzaa, A. A. and El-Meligy, M. M. M. (2006). Synthesis of novel benzofuran and related benzimidazole derivatives for evaluation of *in vitro* anti-HIV-1, anticancer and antimicrobial activities. Arch. Pharm. Res., 29, 826-833. https://www.doi.org/10.1007/bf02973901.

Souza, J. M., Vieira, T. M., Candido, A. C. B. B., Tezykja, D. Y., Rao, S., Albuquerque, S., Crotti, A. E. M., Siqueira-Neto, J. L. and Magalhães, L. G. (2021). *In vitro* anti-*Trypanosoma cruzi* activity

enhacement of curcumin by its monoketone tetramethoxy analog diveratralaceton. Curr. Res. Parasitol. Vector Borne Dis., 1, e10003. https://www.doi.org/10.1016/j.crpvbd.2021.100031.

Summers, S., Bhattacharyya, T., Allan , F., Stothard, R., Edielu, A., Webster, B. L., Miles, M. A. and Bustinduy, A. L. (2022). A review of the genetic determinants of praziquantel resistance in *Schistosoma mansoni*: Is praziquantel and intestinal schistosomiasis a perfect match? Front Trop Dis 3, 933097. https://www.doi.org/10.3389/fitd.2022.933097.

Vasconcelos, M. A., Arruda, F. V. S., de Alencar, D. B., Saker-Sampaio, S., Albuquerque, M. R. J. R., dos Santos, H., Bandeira, P. N., Pessoa, O. D. L., Cavada, B. S., Henriques, M., Pereira, M. O. and Teixeira, E. H. (2014). Antibacterial and antioxidant activities of derriobtusone A isolated from *Lonchocarpus obtusus*. BioMed Res. Int., 2014, 248656. https://www.doi.org/10.1155/2014/248656.

Wang, L., Wu, X., Li, X., Zheng , X., Wang, F., Qi, Z., Huang, M. and Zou, Y. (2020). Imported schistosomiasis: A new public health challenge for China. Front Med, 7, 553487. https://www.doi.org/10.3389/fmed.2020.553487.

Xu, J., Dong, L.-L., Sun, H., Huang, P., Zhang, R.-Z., Wang, X.-Y., Sun, D.-Q. and Xia, C.-M. (2023). Small change, big difference: A promising praziquantel derivative designated P96 with broad-spectrum antischistosomal activity for chemotherapy of schistosomiasis japonica. PLoS Negl Trop Dis, 17, e0011215. https://www.doi.org/10.1371/journal.pntd.0011215.

Yang, L., Lei, H., Mi, C.-G., Liu, H., Zhou, T., Zhao, Y.-L., Lai, X.-Y., Li, Z.-C., Song, H. and Huang, W.-C. (2011). Synthesis, antiproliferative activities and *in vitro* biological evaluation of novel benzofuransulfonamide derivatives. Bioorg. Med. Chem. Lett., 21, 5389-5392. https://www.doi.org/10.1016/j.bmcl.2011.07.007.

Yu, Q.-F., Zhang, J.-Y., Sun, M.-T., Gu, M.-M., Zou, H.-Y., Webster, J. P. and Lu, D.-B. (2021). *In vivo* praziquantel efficacy of *Schistosoma japonicum* over time: A systematic review and meta-analysis. Acta Trop., 222, 2326-2329. https://www.doi.org/10.1016/j.actatropica.2021.106048

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