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LETTER

Flavopereirine Suppresses the Progression of Human Oral Cancer by Inhibiting the JAK-STAT Signaling Pathway via Targeting LASP1 [Letter]

Vidak Raičević

Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia

Correspondence: Vidak Raičević, Faculty of Medicine, University of Novi Sad, Hajduk Veljkova 3, Novi Sad, 21000, Serbia, Email vidak.raicevic@mf.uns.ac.rs

Dear editor

I would like to express serious concerns regarding the article "Flavopereirine Suppresses the Progression of Human Oral Cancer by Inhibiting the JAK-STAT Signaling Pathway via Targeting LASP1" by Xu, Wu & Huang that appeared in Drug Design, Development and Therapy in 2021.[1] The investigations into the antiproliferative activity of flavopereirine on various cancer cells in both in vitro and in vivo models have recently intensified.[2–5] This indoloquinolizinium species is commonly cited as a component of the bark of *Geissospermum laeve* (Vell). Miers,[6] but it is more likely an artefact of the bark extraction process.[7] The structure of flavopereirine was determined in 1957 based on chemical transformations, whereupon it was isolated as a crystalline solid in its betaine form (**1**, Figure 1).[8] Flavopereirine perchlorate (or, more precisely, flavopereirinium perchlorate, **2**, Figure 1) seems to be the salt of choice for studies on the biological activity of flavopereirine,[4,5,9] and is commonly offered by suppliers, presumably due to the contemporary purification methods applied and favorable solubility. The perchlorate counterion is not derived from the natural plant material, as the authors claim in the introduction.

While a lack of terminological rigor is disappointing and can help promote further ambiguities, the article is presented in such a way that one can seriously doubt that any of the observed effects on oral cancer cell lines can be attributed to a species of flavopereirine. While the introduction mentions flavopereirine perchlorate, the authors claim that the chemical used in the assays was "flavopereirine (monohydrate, purity >98%)" purchased from an obscure chemical company. To the best of my knowledge, no chemical company offers the betaine hydrate form of this compound. Moreover, yet a third identity of the compound tested is presented to the reader upon inspection of Figure 1; the presented structure is indeed not a species of flavopereirine, but berberine, a different alkaloid completely lacking the indole system. Not only is it necessary to have the exact molecular formula of the compound used to express molar concentrations correctly, but after the mention of three contrasting identities for the sample tested, one can hardly be certain of the validity of any of the conclusions this investigation put forth.

It would, therefore, always be advisable that researchers independently verify and demonstrate the authenticity of any sample, wherever sourced, used as a starting point for exhaustive investigations of biological activities and underlying mechanisms, especially for the most promising of candidates, as in cases like this one it is impossible to corroborate the validity of any of the presented results in the absence of such evidence.

Disclosure

The author reports no conflicts of interest in this communication.

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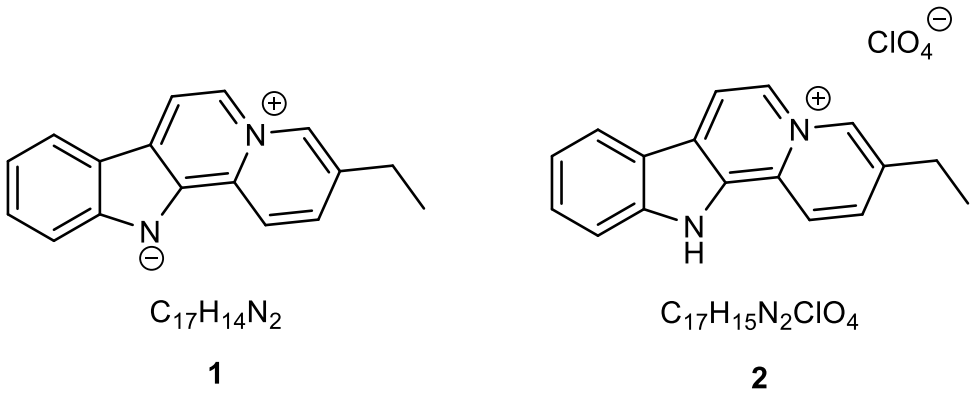

Figure 1 The structures and molecular formulas of flavopereirine betaine (**1**) and flavopereirine perchlorate (**2**).

References

1. Xu J, Wu Z, Huang J. Flavopereirine suppresses the progression of human oral cancer by inhibiting the JAK-STAT signaling pathway via targeting LASP1. *Drug Des Devel Ther*. 2021;15:1705–1716. doi:10.2147/DDDT.S284213
2. Wu J, Lee C, Li Y, et al. Flavopereirine exerts anti-cancer activities in various human thyroid cancer cells. *Am J Cancer Res*. 2024;14(7):3317–3334. doi:10.62347/MINX1330
3. Chen S, Chao C, Huang H, et al. Flavopereirine Inhibits hepatocellular carcinoma cell growth by inducing cell-cycle arrest, apoptosis and autophagy-related protein expression. *Anticancer Res*. 2020;40:6907–6914. doi:10.21873/anticanres.14714
4. Liu J, Fang T, Li M, et al. Pao pereira extract attenuates testosterone-induced benign prostatic hyperplasia in rats by inhibiting 5α-reductase. *Sci Rep*. 2019;9:19703. doi:10.1038/s41598-019-56145-z
5. Yeh H, Tsai Y, Chen M, et al. Flavopereirine induces cycle arrest and apoptosis via the AKT/p38/MAPK/ERK1/2 signaling pathway in human breast cancer cells. *Eur J Pharmacol*. 2019;863:172658. doi:10.1016/j.ejphar.2019.172658
6. Marques DA, Zanchi FB, Evaristo GPC. Ethnopharmacological review, phytochemistry and bioactivity of the genus *Giessospermum* (Apocynaceae). *Res Soc Dev*. 2023;12:e18912240047.
7. Ahamada K, Benayad S, Poupon E, et al. Polyneuridine aldehyde: structure, stability overviews and a plausible origin of flavopereirine. *Tetrahedron Lett*. 2016;57:1718–1720. doi:10.1016/j.tetlet.2016.03.019
8. Hughes NA, Rapoport H. Flavopereirine, an Alkaloid from *Geissospermum vellosii*. *J Am Chem Soc*. 1958;80:1604–1609. doi:10.1021/ja01540a024
9. Miskolczy Z, Megyesi M, Biczók L, Görner H. Effect of electrolytes, nucleotides and DNA on the fluorescence of flavopereirine natural alkaloid. *Photochem Photobiol Sci*. 2011;10:592–600. doi:10.1039/c0pp00367k

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