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SHORT COMMUNICATION

Antiproliferative potential of 3β,5α,6β,7α-tetrahydroxyergosta-8(14),22-diene produced by *Acremonium persicinum* isolated from an alkaline crater lake in Puebla, Mexico

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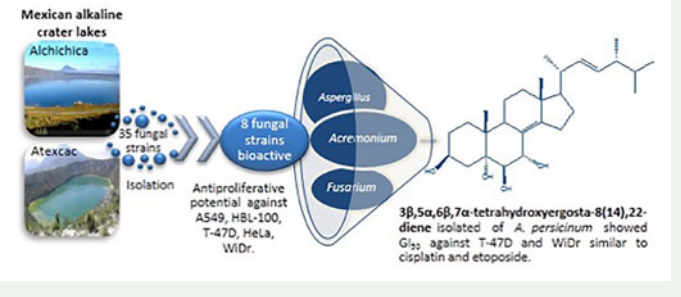
ABSTRACT

The sterol 3β,5α,6β,7α-tetrahydroxyergosta-8(14),22-diene was obtained from bio-guided fractioning of the chloroform extract of 50 L of liquid culture of *Acremonium persicinum*. This fungal strain was selected because of its anti-proliferative activity against solid human tumour cell lines ($GI_{50} \leq 50$ μg/mL) in a bio-prospective study of fungi isolated from plant material, sediment and water samples obtained from alkaline lakes Alchichica and Atexcac in Puebla, Mexico. This compound showed GI_{50} (μM) values of: 16, 24, 18, 15 and 12 against tumour cell lines A-549, HBL-100, HeLa, T-47D and WiDr respectively. GI_{50} effects against tumour lines T-47D and WiDr were found to be greater than the clinically used drugs Etoposide and Cisplatin. Because of this, the results obtained support the pharmacological importance of the microorganisms that develop in these ecosystems and strengthen the non-invasive bio-prospection studies that our work group has developed in recent years.



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1. Introduction

Fungal metabolites have gained importance in the last few decades in the search for new substances with pharmacological benefits (Rateb and Ebel 2011). Adaptation to external adverse factors compared to those in which terrestrial fungi develop (salinity, absence of solar radiation, low temperature, high hydrostatic pressure, alkalinity) can lead to the production of unique chemical substances with anticancer properties (Deshmukh et al. 2018). Examples of it, are Acremoline and Cordyheptapeptides C-E, obtained from *Acremonium strictum* and *A. persicinum* strains isolated from marine samples and that showed activity against several cancer cell lines (Chen et al. 2012; Julianti et al. 2012).

In this sense and following the search for bioactive compounds produced by fungi from aquatic ecosystems, we isolated a sample of *Acremonium persicinum* during the bio-prospecting study of the sediment of lake Alchichica and found that its extract inhibited the growth of several human solid tumour cell lines. Therefore, in this paper we report on the isolation and structural characterisation of sterol 3β,5α,6β,7α-tetrahydroxyergosta-8(14),22-diene, as a bioactive natural product obtained from the screening of fungi with antiproliferative activities isolated from alkaline lakes Alchichica and Atexcac in Puebla, Mexico.

2. Results and discussion

From the screening search for bioactive fungi from the alkaline lakes Alchichica and Atexcac, 35 genera of fungi were isolated and identified according to their morphological and microscopic characteristics. Among them, eight fungal species were found to be bioactive and phylogenetically identified (Supplementary material Figure S1). Antiproliferative activity of the biomass extract and culture broth of each of the eight fungal strains capable of inhibiting cell proliferation ($GI_{50} \leq 50\ \mu g\ mL^{-1}$) of the tested cancer lines are summarised in supplementary material Table S1. From the results described above, the antiproliferative potential manifested by the extracts of *Acremonium persicinum* against all tested cancer cell lines is highlighted.

Following the bio-guided fractioning of the mass culture of *Acremonium persicinum*, a compound with high anti-proliferative activity against the human solid tumour cell lines (A-549, HBL-100, HeLa, T-47D and WiDr) was obtained. Purified from the chloroform extract of the biomass produced in a 50 L liquid culture medium , the compound was identified using its ^{1}H and ^{13}C NMR spectroscopic data as 3β,5α,6β,7α-tetrahydroxyergosta-8(14),22-diene (Supplementary material Figure S2) (**1**) , which coincided with a previous report (Zhang et al. 2016). In addition, ergosterol (**2**) (Trigos and Ortega-Regules 2002), ergosterol peroxide (**3**) (Ramos-Ligonio et al. 2012) and cerevisterol (**4**) (Mendoza et al. 2015) were also isolated from the same extract.

The sterol (**1**), reported previously, had been isolated from microscopic fungus *Penicillium* sp. found in marine environment, and showed strong activity against cell line Hep G, with IC_{50} of 10.4 μg/mL (Sun et al. 2006). Similarly, it was obtained from bacteria *Streptomyces anandii* manifesting inhibitory effect against cell lines MCF-7 (27.4 μg/mL), SF-268 (25.1 μg/mL) and NCI-H460 (23.7 μg/mL) (Zhang et al. 2016). This compound was also isolated from a sample of *Pleurotus cornucopiae* in Korea, showing

renoprotective activity while in the presence of cisplatin, reducing nephrotoxicity of the latter by 80% (Lee et al. 2017). It is worth mentioning that the other sterols (**2**–**4**) found in this study have also been reported for their biological activities (Suárez-Medellín et al. 2014).

The compound (**1**) had no previous reports on bioactivity against solid human tumour cell lines A-549, HBL-100, HeLa, T-47D and WiDr. In this study we obtained GI_{50} values (μM): 16, 24, 18, 15 and 12, respectively. This compound's GI_{50} values against T-47D and WiDr cell lines (breast and colon cancer) proved to be lower than those of current commercial drugs etoposide and cisplatin (Trigos et al. 2013), providing a pharmacological alternative to help in the treatment of these cancers.

3. Experimental

Experimental section, Figure S1, Figure S2 and Table S1 detailed in supplementary material.

4. Conclusion

We report on the antiproliferative potential of (**1**) produced by *A. persicinum*, remarking on its similar or even more potent effect against breast and colon cancer cell lines T-47D and WiDr than those of drugs commonly used in anticancer therapy. We also indicate that these alkaline aquatic environments withhold great biological and pharmacological potential, adding further reasons for promoting its ecological significance and protection. Therefore, not only does this study prove the presence of bioactive fungi in lakes Alchichica and Atexcac, it also offers a perspective for further investigation of bioactive fungal strains in other Mexican alkaline lakes.

Disclosure statement

No potential conflict of interest was reported by the authors.

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