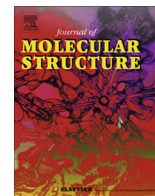


Contents lists available at ScienceDirect

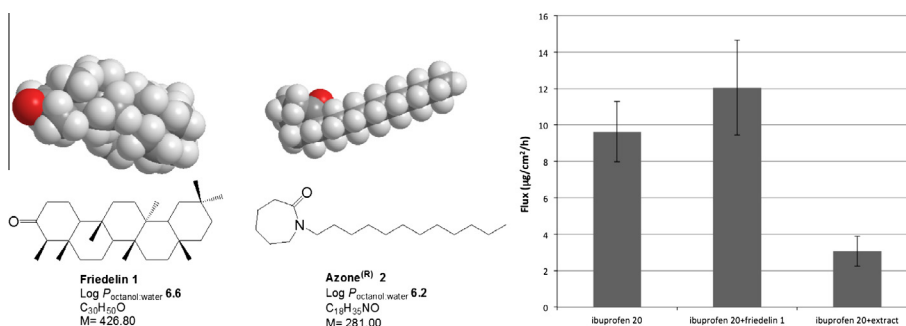
Journal of Molecular Structure

journal homepage: www.elsevier.com/locate/molstrucNovel insights for permeant lead structures through *in vitro* skin diffusion assays of *Prunus lusitanica* L., the Portugal LaurelMaria do Céu Costa^{a,b,*}, Patrícia Duarte^a, Nuno R. Neng^c, José M.F. Nogueira^c, Filomena Costa^d, Catarina Rosado^a^a CBIOS, Universidade Lusófona, Campo Grande, 376, 1749-024 Lisboa, Portugal^b LNEG, Laboratório Nacional de Energia e Geologia, I.P., Estrada da Portela, Bairro do Zambujal, Apartado 7586, Alfragide, 2610-999 Amadora, Portugal^c Universidade de Lisboa, Faculdade de Ciências, Departamento de Química e Bioquímica e Centro de Química e Bioquímica, Campo Grande, 1749-016 Lisboa, Portugal^d ASAE – Autoridade de Segurança Alimentar e Económica, Departamento de Riscos Alimentares e Laboratoriais (DRAL), Edifício F – Estrada do Paço do Lumiar, 1649-038 Lisboa, Portugal

HIGHLIGHTS

- The *P. lusitanica* L. extract has a novel effect of retarding permeation of both lipophilic and hydrophilic model molecules.
- Terpenes were identified by GC–MS after extraction by ASE (50.55%) and Soxhlet (89.91%) using the same solvent (PE 40–60 °C).
- The ability of a triterpene to act as a promotor of the permeation of ibuprofen was herein determined for the first time.
- It was concluded that permeation enhancement capacity is linked to the lipophilic properties of friedelin.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:

Received 30 May 2014

Received in revised form 8 August 2014

Accepted 14 August 2014

Available online 23 August 2014

Keywords:

Prunus lusitanica L. constituents

Permeant model

Skin barrier

Friedelin

Ibuprofen **20**Caffeine **19**

ABSTRACT

As a contribution for the generation of libraries in which a natural product (NP) is used as the guiding structure, this work sought to investigate molecular features of triterpenes as deliver leads to cross the *stratum corneum* at a significant rate. Seeking a bioguided investigation of the dermocosmetic lead-like potential of triterpenes in *Prunus lusitanica* L., various extracts were obtained by two different methods (Soxhlet extractor and Accelerated Solvent Extraction–ASE) and analyzed by GC–MS and NMR. *In vitro* assays were conducted to quantify the friedelin **1** and crude plant extract permeation through a membrane of polydimethylsiloxane (PDMS), as well as their skin penetration enhancement capacity using two model molecules, caffeine **19** and ibuprofen **20**. Friedelin **1** was identified as the major component (16–77%, GC) with isolated yield of 51% w/w (94%, GC) from Soxhlet residue (1.7% p/p) of the dried aerial parts of the plant harvested when in early flowering stage. Friedelin **1** promoted the penetration of the lipophilic molecule **20**, however, it did not influence the permeation of the hydrophilic permeant **20**. On the other hand, the crude extract acted as a retardant of the penetration of both substances. Molecular characteristics for the applicability of *P. lusitanica* L. in the development of dermocosmetics, as well as a new potential use for friedelin **1** in particular, are demonstrated. Probable mechanisms for chemical penetration enhancement using triterpenes as models for transdermal administration are herein discussed.

© 2014 Elsevier B.V. All rights reserved.

* Corresponding author at: CBIOS, Universidade Lusófona, Campo Grande, 376, 1749-024 Lisboa, Portugal. Tel.: +351 21 0924691; fax: + 351 214720203.

E-mail addresses: p1658@ulusofona.pt, ceu.costa@lneg.pt, 214720203@fax.ptprime.pt (M.C. Costa).