THE INFLUENCE OF CHEMICAL STRUCTURE IN THE DRUG RELEASE OF TWO MODULATED FLAVANONES FORMULATED IN A NANO SYSTEM

P. Bustos-Salgado[1], B. Andrade Carrera[2], V. Dominguez-Villegas[2], A. Calpena Campmany[1,3], M.L. Garduño-Ramírez [4]

[1]Departament de Farmàcia i Tecnologia Farmacèutica i Departament de Fisicoquímica de la Facultad de Farmàcia i Ciencies de la Alimentaciò, Universitat de Barcelona; Avda Joan XXIII, 27-31 08028, Barcelona, España. [2] Facultad de Ciencias Químicas e Ingeniería, Universidad Autónoma del Estado de Morelos; Av. Universidad 1001, Cuernavaca, Morelos, México. [3] Instituto de Nanociencia y Nanotecnología (IN2UB), Universitat de Barcelona, España. [4]Centro de Investigaciones Químicas, Instituto de Investigación en Ciencias Básicas y Aplicadas, Universidad Autónoma del Estado de Morelos; Av. Universidad 1001, Cuernavaca, Morelos, México.

INTRODUCTION

Prenylated flavanones include a diverse class of naturally flavonoids oxygen-containing heterocycles that contain prenyl substituents. Nowadays many studies proved their anti-oxidative, anti-obesity, anti-inflammatory and other various biological effects that could apply in the prevention of various pathologies including cancer [1-3]. Recently, the flavanone (2*S*)-5,7-dihydroxy-6-(3-methyl-2-buten-1-yl)-2-phenyl-2,3-dihydro-4H-1Benzopyran-4-one **1** was isolated from a methanol extract obtained from the aerial parts of *E. platycarpa* [4].

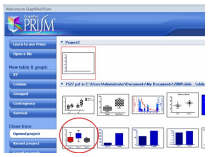
MATERIAL AND METHODS

Nano system formulation

0.5% w/w of **2** and **3**
Labrasol, labrafac, plurol oleique and propylene glycol

Particle Size

Dynamic Light Scattering. Zeta-Sizer, Malvern Instruments



Data analyzed by GraphPad Prism software (Weibull model)

In vitro study

Franz Diffusion Cells: **dialysis membrane**. Sink conditions. The donor side: 0.3 mL of **NSF 2** and **NSF 3**. Receptor phase: EtOH:H_2O (70:30). The diffusion area : 2.54 cm^2. Samples were withdrawn at different time point scheme for 89 h (n = 3).

PURPOSE

The aim of this study was to evaluate a new topical emulsion that contained the prenyl flavanones (8S)-5-hydroxy-2,2-dimethyl-8-prenyl-3,4,7,8-tetrahydro-2H,6H-Benzo[1,2-b:5,4-b˙]dipyran-6-one **2**; and (8S)-5-hydroxy-2,2-dimethyl-8-phenyl-7,8-dihydro-2H,6H-Benzo[1,2-b:5,4-b˙]dipyran-6-one **3** (Figure 1) in a nano system formulation (**NSF**) through *in vitro* drug release.

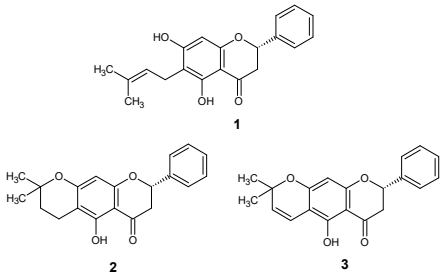


Figura 1. (2*S*)-5,7-dihydroxy-6-(3-methyl-2-buten-1-yl)-2-phenyl-2,3-dihydro-4H-1Benzopyran-4-one **1**; (8S)-5-hydroxy-2,2-dimethyl-8-prenyl-3,4,7,8-tetrahydro-2H,6H-Benzo[1,2-b:5,4-b˙]dipyran-6-one **2**; and (8S)-5-hydroxy-2,2-dimethyl-8-phenyl-7,8-dihydro-2H,6H-Benzo[1,2-b:5,4-b˙]dipyran-6-one **3**.

HPLC

H_2O:AcN (20:80) for **2** and (10:90) for **3** as mobile phase; 1 ml/min flow rate; 300 nm. Column: EC250/4.6 Nucleosil 100-5 mm C18 Macherey-Nagel [5].

RESULTS

The average drop size of the nanostructured formulation of **2** and **3** were 340,6 and 383 nm with PI = 0.2 and 0.4 respectively. The kinetic release model that best describes the amount of (**2** and **3**) load at any time is representing by the function named as Weibull,

$$Q_t = Q_\infty \left[1 - e^{-\left(\frac{t}{t_d}\right)\beta}\right]$$

Table 1. Weibull parameters for formulation 2 and 3.

	NSF 2	NSF 3
Q (µg)	1714 ± 556.2	48.4 ± 16.1
t_d (h)	83.6 ± 25.5	41.5 ± 33.2

CONCLUSIONS

Although the similar drop size of both nano structured formulation, the kinetic release of the formulation showed a significant difference. While, Q represents the maximum quantity at which release tends; t_d is the time at which 63 % of the initial amount of flavanone tested has dissolved. The flavanone **2** release more than flavanone **3** maybe due to the absence of double bond in **3**. The nano-structured formulation of flavanones **2** and **3** are promising alternatives to administrate modified drug.

ACKNOWLEDGE

Acknowledge to CONACyT, Mexico for the scholarship 709906 and Gattefossé for supplying excipients for this study.

CONTACT PERSON

paola2006@hotmail.com,
bereniceac@uaem.mx,
valeri.dominguez@uaem.mx,
anacalpena@ub.edu,
lgarduno@uaem.mx

REFERENCES

[1] M.S. Brewer, *Compr. Rev. Food Sci. Food Saf.* **2011**, 10: 221–247.
[2] S. Venturelli, *et al*, Nutrition. **2016**, 32: 1171–1178.
[3] X. Yang, *et al. Trends Food Sci. Technol.* **2015**, 44: 93–104.
[4] V. Domínguez-Villegas; *et al*, *Nat. Prod. Comm.*, **2013**, 8:177-180.
[5] P. Bustos-Salgado, *et al*, *Biomolecules*, **2020**, 10(6): 889.