

## EFFECT ON RAT BLOOD PRESSURE OF EPITAONDIOL, DITERPENOID ISOLATED FROM THE ALGAE *STYPOPODIUM FLABELLIFORME* OF RAPA NUI (CHILEAN ISLAND TERRITORY IN THE PACIFIC OCEAN)

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### Abstract

Easter Island is an island territory of Chile located in the middle of the Pacific Ocean. It is characterized by a great maritime wealth and endemism. We worked with a epitaondiol compound, isolated from the alga *Stytopodium flabelliforme*, which is also producer of a number of secondary metabolites. In this article, the effect of mono- and di epitaondiol acetate was studied on blood pressure in normotensive rats. The results are important but do not show significant difference as antihypertensive, but the recovery period is prolonged. These results prove to be pioneers in the study on blood pressure of chemical compounds isolated from Easter Island algae.

**Keywords:** Chile, Easter Island, *Stytopodium flabelliforme*, Epitaondiol, Mean arterial pressure.

## Introduction

Rapa Nui (in pascuence language), Isla de Pascua (in spanish) or Easter Island (in English), is a Chilean island located in Polinesia in the Pacific Ocean with coordinates: 27°7'10"S, 109°21'17"O. It is characterized by a great maritime wealth characterized and endemism. Continuing the study of marine natural products of Easter Island, the algae *Styopodium flabelliforme* Weber van Bosse (family Dicitaceae) collected on the beaches of Hanga Roa was studied. This family of algae is characterized by producing a variety of secondary metabolites with different biological activity [1, 2, 3, 4, 5, 6, 7]. *S. flabelliforme* presents many similarities with the algae *Styopodium zonale* [8] which have recently isolated new compounds [9]; *S. zonale* extract was studied in human metapneumovirus activity [10]. The major compounds found in *S. flabelliforme* were mixed biogenesis terpenes, diacetyl and triacetyl epitaondiol [1]. In the search for new drugs of marine natural origin, we previously studied the effect of diacetyl epitaondiol in both cardiovascular level atrium and isolated rat aorta [11]. In atrium, the effect on the strength and frequency of spontaneous contraction and aorta, which has been extensively studied by our group [12, 13]. It was studied the role of endothelium in modulating the vascular response to contractile agents and relaxers. Recently, we published a pharmacological study of norsiphonarienone, isolated from the mollusk *Siphonaria lessoni* [13]. Continuing the marine natural products study and algae *Styopodium flabelliforme* Weber van Bosse, in this article we communicate the results of epitaondiol monoacetate and diacetate epitaondiol (Figure 1) on blood pressure in normotensive rats.

## Methods

### Algal Collection

The brown alga, *Styopodium flabelliforme*, was collected intertidally near the Hanga Roa beach in Easter Island (South Pacific), V Región, Chile, in 2005 at a depth of 5-10 m. A voucher specimen was deposited in the Museo Nacional de Historia Natural, Santiago, Chile and the identity was confirmed by Prof. M. Eliana Ramirez from the Museo de Historia Natural de Santiago.

### Extraction and Isolation

Wet specimens (2.0 kg) were frozen for transportation and later repeatedly extracted with dichloromethane (CH<sub>2</sub>Cl<sub>2</sub>) to produce 60.5 g of crude organic extract and then, it was subsequently acetylated with acetic anhydride-pyridine. A portion

of the extract was purified by repeated column chromatography on silica gel using an n-hexane/EtOAc/MeOH gradient. By further treatment with base the following compounds Isoepitaondiol 2 (10 mg), epitaondiol 3 (1 g), styodiol 4 (200 mg) and styoptriol 6 (1.1 g) were obtained of this extract.

### Animal studies

Adult normotensive white rats of the Sprague Dawley strain (200-300 g) of both sexes were anesthetized with Nembutal (50 mg / kg i.p.). Then the rat was placed in supine position on a thermo regulated table. Vein and the femoral artery cannulated with PE 90 polyethylene and PE 10 Clay Adams, respectively with the help of a magnifying glass Nikon 104653 and lighting through a lamp optical waveguides Schott KL 1500, to prevent desiccation of the exposed tissue. Through the vein, the vehicle and the drug were infused. The artery was connected to a pressure transducer Gould model P23-ID. Rectal temperature control was performed through a tele thermometer Simpson Electric throughout the experiment.

## Results

The results show that both epitaondiol monoacetate and epitaondiol diacetate (Figure 1), not significantly affect blood pressure decreases possibly no altering any organ system in the animal studied, presenting epitaondiol monoacetate in a concentration greater 10<sup>-3</sup> mM an effect of only 10% (Table 1).

While the answers are not significant, the recovery time is prolonged implying that could be useful in processes requiring mild cardiac output. It is curious that the recovery of the pressure after the administration of drugs present an effect more responsive to the control (Table 2). This would imply that these compounds of marine origin produce some kind of physiological alteration at the blood level, opening a new door for future studies.

## Discussion

Hypertension is one of the most important public health problems, being the most common cause of cardiovascular mortality. In Chile, cardiovascular diseases account for between 20 and 50% of all deaths. Reno vascular hypertension (2-5% of cases) is the most common curable cause of secondary hypertension [14]. Treatment with pharmacotherapy, has had a relative success in controlling hypertension due to adverse reactions, therefore has encouraged the search for alternative treatments. *Styopodium flabelliforme* is an alga that grows on islands such as Easter Island. It is

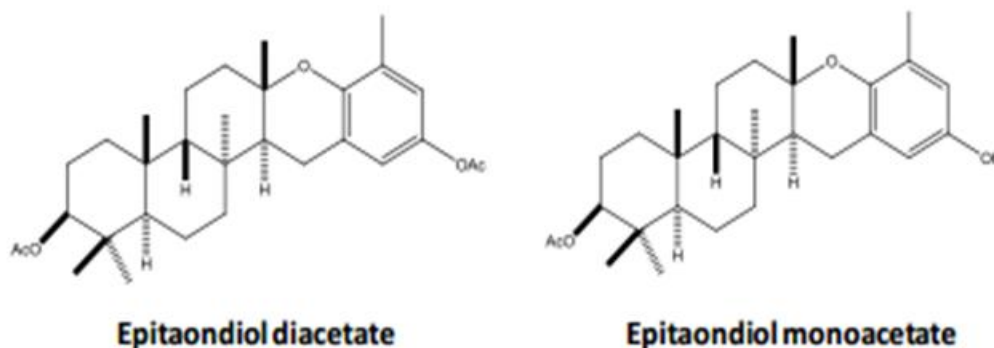
characterized by the presence of chemical structures such as epitaondiol, which is obtained in very low amounts which fails to develop full pharmacological studies. The purpose of this study was to expand our knowledge of the pharmacological effects of epitaondiol and try to establish a scientific basis for potential use. The results obtained while important, are not encouraging for further study of this effect. While it was determined the effect of epitaondiol diacetyl on blood pressure in normotensive rats [15] preliminarily, this study corroborated these results and likewise try to complete the basis of previous results at cardiovascular level since diacetyl because epitaondiol produces a negative inotropic action on the order of 35% ( $10^{-3}$  M) [11], which would base the effect on blood pressure being due to a decrease in cardiac output and it relates to other pharmacological properties that have been studied [16].

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**Figure 1.** Shows the chemical structures of epitaondiol diacetate and monoacetate, both compounds isolated from the algae *Styopodium flabelliforme* at Eastern Island.

**Table 1.** Shows the results of two concentrations epitaondiol monoacetate and one of diacetate on the mean arterial pressure (MAP), control and experimental, the latter in the presence of the respective compound. Also, the percent decrease of the hypertensive effect. Results expressed as Mean  $\pm$  standard deviation (SD).

	Concentration n mM	MAP Control	MAP experimental	▲ MAP	MAP % decrease
Epitaondiol Monoacetate	10 <sup>-3</sup>	98.1 $\pm$ 3.5	86.5 $\pm$ 4.0	11.6	11.8%
	10 <sup>-4</sup>	103.4 $\pm$ 3.5	100.7 $\pm$ 3.6	2.7	2.6%
Epitaondiol Diacetate	10 <sup>-3</sup>	92.6 $\pm$ 2.3	88.3 $\pm$ 2.2	4.3	4.6%

**Table 2.** Shows the results of two concentrations epitaondiol monoacetate and one of diacetate on the time for the maximal effect (Max Effect, sec), MAP recovery, and the time of recovery from the initial state or control. Results expressed as Mean  $\pm$  standard deviation (SD).

	Concentration mM	Max Effect (sec)	MAP Recovery	Recovery Time (sec)	n
Epitaondiol Monoacetate	10 <sup>-3</sup>	88.9 $\pm$ 8.6	95.6 $\pm$ 3.5	85.6 $\pm$ 8.9	11
	10 <sup>-4</sup>	87.8 $\pm$ 14.6	103.6 $\pm$ 3.6	90.3 $\pm$ 14.3	6
Epitaondiol Diacetate	10 <sup>-3</sup>	103.0 $\pm$ 8.3	92.4 $\pm$ 2.2	93.8 $\pm$ 8.4	7