

## Preliminary Pharmacological Studies on three Benzoyl Amides, constituents of *Aniba riparia* (Nees) Mez (Lauraceae)

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**SUMMARY.** Pharmacological screening of methyl ethers of *N*-benzoyltyramine (riparin I), *N*-(2-hydroxybenzoyl)-tyramine (riparin II) and *N*-(2,6-dihydroxybenzoyl)-tyramine (riparin III), obtained from *Aniba riparia* was performed. The compounds given orally (p.o.) or intraperitoneally (i.p.) in doses up to 1 g/kg caused no deaths in mice, except riparin III which was toxic by the i.p. route; lethal dose 50% (LD50) was 104.2 mg/kg. Riparin I and riparin II (500 mg/kg i.p. and p.o.), and riparin III (500 mg/kg p.o. or 35 mg/kg i.p.) were without effects in the screening for behavioural changes in mice. Riparin I, riparin II and riparin III induced nonspecific and reversible relaxation of contractions produced by acetylcholine and histamine in the guinea-pig ileum and by oxytocin and bradykinin in the rat uterus. The inhibitory concentration 50% (IC50 values) varied from 1.7-5.0 µg/ml. Riparin III was, in general, twice as potent as riparin I and riparin II, which were about equipotent. Riparin III also relaxed the guinea-pig trachea (IC50 = 1.9 µg/ml). In the rat phrenic nerve-diaphragm preparation, the compounds inhibited muscle twitches induced by either direct or indirect electrical stimulation (IC50 = 4.0 and 2.4 µg/ml, respectively, for riparin III).

**RESUMEN.** "Estudios Farmacológicos Preliminares sobre Tres Benzoilamidas constituyentes de *Aniba riparia* (Nees) Mez (Lauraceae)". Se realizaron estudios farmacológicos de éteres metílicos de *N*-benzoiltiramina (riparina I), *N*-(2-hidroxibenzoil)-tiramina (riparina II) y *N*-(2,6-dihidroxibenzoil)-tiramina (riparina III), obtenidos de *Aniba riparia*. Los compuestos administrados por vía oral (v.o.) o intraperitoneal (i.p.) en dosis de hasta 1g/kg no causaron la muerte de ratones, excepto riparina III, que resultó tóxico por la vía i.p. (DL50 = 104,2 mg/kg). Riparina I y riparina II (500 mg/kg i.p. y v.o.) y riparina III (500 mg/kg v.o. o 35 mg/kg i.p.) no presentaron efectos sobre cambios de comportamiento en ratones. Riparina I, riparina II y riparina III provocaron, de forma no específica y reversible, relajamiento de las contracciones producidas por acetilcolina e histamina en el íleo de ratón y por la ocitocina y bradiquinina en el útero de rata. Los valores de CI50 variaron de 1.7-5.0 µg/ml. Generalmente riparina III fue dos veces más potente que riparina I y riparina II, que fueron de igual potencia. Riparina III también causó relajamiento de la tráquea de ratón (CI50 = 1,9 µg/ml). Los compuestos también inhibieron las contracciones del diafragma de ratón, producidas por estimulación eléctrica directa o indirecta (CI50 = 4,0 y 2,4 µg/ml, respectivamente, para riparina III).

### INTRODUCTION

The genus *Aniba* comprises 41 species of shrubs and trees and is primarily a lowland group with its centre of diversity in Central Amazonia and Guiana. It extends, however, into the Andes, the mountains of northern Venezuela, the lesser Antilles and eastern and southern Brazil. *Aniba riparia* (Nees) Mez, a Lauraceous

tree popularly known as "louro", occurs in the Humaitá region of the Amazonas state of Brazil<sup>1</sup>.

Methyl ethers of *N*-benzoyl tyramine (riparin I), *N*-(2-hydroxybenzoyl) tyramine (riparin II) and *N*-(2,6-dihydroxybenzoyl) tyramine (riparin III) with broad spectrum antimicrobial activity have been isolated from the unripe fruit of *Aniba riparia*<sup>1</sup> and later synthesised by Barbosa-

**KEY WORDS:** *Aniba riparia*, Lauraceae, Methyl ethers of *N*-benzoyltyramine, Smooth and skeletal muscle relaxation.

**PALABRAS CLAVE:** *Aniba riparia*, Lauraceae, Éteres metílicos de *N*-benzoiltiramina, Relajamiento del músculo liso y esquelético.

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