III SIMPÓSIO INTERNACIONAL EM INVESTIGAÇÕES QUÍMICO-FARMACÊUTICAS
I ENCONTRO IBERO-AMERICANO DE PLANTAS MEDICINAIS DR. MAHABIR GUPTA
I CONGRESSO LUSO-BRASILEIRO DE CIÊNCIAS E TECNOLOGIAS EM SAÚDE

Área: QMC 02

SYNTHESIS OF NEW BENZIMIDAZOLE DERIVATIVES. IN VITRO EVALUATION OF ITS ANTIPROTOZOAL ACTIVITY

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INTRODUCTION

The benzimidazole nucleus (BZ) is one of the most promising heterocyclic moieties that has yielded several successful drugs with different applications in medicinal chemistry, with antimicrobial activity, among others [1]. Human parasitic diseases transmitted by vectors constitute a major health problem, which represent more than 17% of all infectious diseases and cause more than 700,000 deaths each year. The most affected populations are those living in tropical and subtropical regions, and specifically the poorest communities [2]. Some of these diseases are caused by protozoa such as *Plasmodium* spp., *Trypanosoma* spp. or *Leishmania* spp. The high toxicity and drug resistance to established drugs lead to therapeutic failure [3, 4]. Therefore, new therapeutic hits are needed. The aim of this work was to obtain different BZ derivatives, and to evaluate their antiprotozoal activity.

MATERIAL AND METHODS

Two BZ families were obtained: 2-phenyl-BZ (I) and 2-arylmethylaminoBZ (II). Compounds type I were obtained by direct treatment of phenylenediamines with aldehydes in the presence of $Na_2S_2O_5$ at 60 - 80 ºC; while type II were synthesized by condensation of 2-aminoBZ, previously obtained, with aldehydes at 120 ºC, followed by reduction with $NaBH_4$.

RESULTS

All compounds were tested at doses of 10 µM, and the percentage of inhibition was calculated. Fifteen type I and five type II compounds showed an inhibition value higher than 85%. Three of type I showed IC_{50s} in the range of 1.86 to 3.50, and were non-toxic. Type II compounds did not show any interesting IC_{50} value.

CONCLUSIONS

More than 30 type I and 25 type II BZ derivatives were obtained, and evaluated *in vitro* against protozoa, obtaining interesting results.

ACKNOWLEDGMENTS

Financial support by grants from MICINN, Spain (PID2019-106222RB-C32/AEI/ 10.13039/5011000-11033) and SENACYT, Panama (FID2017-095) are acknowledged.

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