

**Green strategies against malaria and dengue: larvicidal, antiparasitic and antiviral potential of essential oils from *Piper* species**

André C. de Oliveira<sup>1</sup>, Ingrity Suellen C. Sá<sup>2</sup>, Felipe Moura Araujo da Silva<sup>2</sup>, Glenda Quaresma Ramos<sup>3</sup>, Rosemary Aparecida Roque<sup>1</sup>, Gamilson Soares Pontes<sup>4</sup>, Sergio Massayoshi Nunomura<sup>5</sup>, Rita de Cássia Saraiva Nunomura<sup>2</sup>

<sup>1</sup> Laboratório de Controle Biológico e Biotecnologia da Malária e da Dengue, Instituto Nacional de Pesquisas da Amazônia, 69067-375, Manaus, Amazonas, Brasil

<sup>2</sup> Central Analítica, Centro de Apoio Multidisciplinar, Universidade Federal do Amazonas, 69080-900, Manaus, Amazonas, Brasil

<sup>3</sup> Centro Multiusuário para Análise de Fenômenos Biomédicos, Universidade do Estado do Amazonas, 69065-001, Manaus, Amazonas, Brasil

<sup>4</sup> Laboratório de Virologia, Instituto Nacional de Pesquisas da Amazônia, Manaus, Amazonas, 69067-375, Manaus, Amazonas, Brasil

<sup>5</sup> Laboratório de Princípios Ativos da Amazônia, Instituto Nacional de Pesquisas da Amazônia, 69067-375, Manaus, Amazonas, Brasil  
andrebiologo2011@gmail.com

**Keywords:** Piperaceae; Culicidae; arbovirus; *Plasmodium*

In Brazil, malaria and dengue are diseases caused by *Plasmodium* and DENV, respectively, and primarily transmitted by *Anopheles darlingi* and *Aedes aegypti*, mosquitoes that have developed resistance to insecticides often toxic to non-target organisms. As of May 2025, over 1,242,400 probable cases of dengue and 29,955 confirmed cases of malaria have been reported. In response, eco-friendly vector control strategies have increasingly focused on natural products from Amazonian plants, particularly *Piper* species. This study aimed to investigate the essential oils (EOs) and major compounds from *P. alatipetiolatum* as *P. purusanum* as potential agents against mosquito vectors and the etiologic agents of malaria and dengue. The EOs were extracted by hydrodistillation and characterized using GC-based techniques, while the major compounds were isolated and identified by column chromatography, MS, GC-MS, GC-FID, HPLC, and <sup>1</sup>H and <sup>13</sup>C NMR. These products were evaluated against *An. darlingi* and *Ae. aegypti* larvae, *P. vivax*, and DENV. Toxicity was also assessed in non-target aquatic organisms, including Hemiptera, Coleoptera, and Diptera. All EOs and the compounds 6-ishwarone, ishwarol, ishwarane,  $\beta$ -caryophyllene and piplartine showed larvicidal activity (LC<sub>50</sub> from 29.31 to 40.76  $\mu$ g/mL), with cellular damage and changes in antioxidant enzymes such as SOD, CAT, GST, and  $\alpha$ - and  $\beta$ -esterases. Antiparasitic (IC<sub>50</sub> from 3.7 to 11.2  $\mu$ g/mL) and antiviral (IC<sub>50</sub> from 5.8 to 13.24  $\mu$ g/mL) activities were also observed, with no cytotoxicity to VERO or PBMC cells. These products showed toxicity to non-target organisms only at high concentrations (LC<sub>50</sub> from 2,098.80 to 7,707.13  $\mu$ g/mL), indicating environmental safety. Thus, EOs and compounds from *P. alatipetiolatum* and *P. purusanum* may serve as eco-friendly alternatives for controlling mosquito vectors and the pathogens of malaria and dengue.

**Support:** FAPEAM, CNPq.