

## Epigenetic Modification of Secondary Metabolites Production in *Penicillium* sp.

Nur Syazwatul Iffah Sakari<sup>a</sup>, Siti Hajar Sadiran<sup>ab\*</sup>

### Structured Abstract

**Background:** Secondary metabolites (SMs) in soil fungi especially *Penicillium* sp. are widely researched in the field of medication and have been the center of attention of scientists' interests due to their diverse benefits to humankind. Unfortunately, the fungal gene clusters responsible for synthesizing secondary metabolites for survival in natural environment can remain inactive in unnatural settings, such as laboratory conditions. Therefore, this study two different media along with the elicitation of epigenetic modifiers to activate the cryptic biosynthetic pathways in *Penicillium* sp.

**Methods:** *Penicillium* sp. was cultured on Sabouraud dextrose agar (SDA) and Czapek's Dox agar (CDA), and then incubated at 28°C for 14 days. Subsequently, the difference in the morphology of the *Penicillium* sp. was observed macroscopically and microscopically. Next, the fungus was fermented in Sabouraud dextrose broth (SDB) and Czapek's Dox broth (CDB) with and without epigenetic modifiers, 5-azacytidine (50 µM) and valproic acid (25 µM). The cultures were incubated for two weeks at 28°C. Next, the secondary metabolites were extracted by ethyl acetate using a liquid-liquid extraction method. The dried crude extracts were then subjected to HPLC analysis to observe the effects of the epigenetic modifiers. The chromatogram of the extracts resulting from the fermentation with epigenetic modifiers was examined and compared with the control.

**Results:** This study shows the SDA enhances the growth and sporulation of *Penicillium* sp. The elicitation of epigenetic modifiers in the fungi culture media also increases the yield of the crude extracts. The SDB control and SDB with 5-azaC show similar patterns of HPLC chromatogram. The comparison of the chromatogram showed that valproic acid enhance the production of secondary metabolites of *Penicillium* sp. in CDB (synthetic media) compared to the control and SDB.

**Conclusion:** In conclusion, this study demonstrates that valproic acid successfully enhance the production of secondary metabolites in *Penicillium* sp. in CDB. This is due to fungi's tendency to produce secondary metabolites under a stressful environment. The depletion of nutrients in the CDB could cause environmental stress and increase the production of secondary metabolites.

**Keywords:** 5-azacytidine, Epigenetic Modifiers, *Penicillium* sp., Valproic Acid.

---

\*Correspondence: [hajarsadiran@uitm.edu.my](mailto:hajarsadiran@uitm.edu.my)

<sup>a</sup> School of Biology Faculty of Applied Sciences, Universiti Teknologi MARA, Shah Alam, Malaysia

<sup>b</sup> Atta-ur Rahman Institute for Natural Product Discovery (AuRIns), Universiti Teknologi MARA Selangor, Puncak Alam Campus, Bandar Puncak Alam, Malaysia.