

## INTISARI

Penuaan kulit utamanya disebabkan oleh sinar ultraviolet (UV) menyebabkan hilangnya integritas kulit. Sinar UV menyebabkan over-ekspresi dari penanda penuaan kulit, salah satunya adalah *matrix metalloproteinase 9* (MMP-9) yang merupakan enzim pendegradasi matriks ekstraseluler. Merica hitam memiliki aktivitas sebagai antioksidan, anti-inflamasi, dan anti-*senescence*. Penelitian ini bertujuan untuk menelusuri potensi merica hitam sebagai agen pencegah penuaan dini pada sel fibroblas akibat sinar UV dengan target MMP-9 dan gen target lain yang terlibat. Studi meta analisis bioinformatika dan analisis *machine learning* dilakukan melalui *online databases* dan penggunaan *software*. Pengaruh sinar UV pada patofisiologi penuaan kulit diperoleh melalui penelusuran literatur. Level ekspresi MMP-9 diperoleh melalui *database* The Human Protein Atlas. Gen target terkait penuaan pada sel fibroblas diperoleh melalui *database* Genecards. Profil metabolomik merica hitam diperoleh melalui *database* CMAUP. Potensi inhibitor senyawa merica hitam terhadap MMP-9 diperoleh melalui *software* KNIME dan *database* ChEMBL. Gen target potensial merica hitam diperoleh melalui irisan gen target dari *database* Genecards dan studi literatur. Peran MMP-9 dan gen target terkait diperoleh melalui studi literatur dan *database* KEGG pathway. Hasil penelitian ini menunjukkan bahwa sinar UV meningkatkan level ekspresi MMP-9. Empat kandungan senyawa merica hitam yaitu pinocembrin, piplartin, piperin dan  $\beta$ -caryophyllene menunjukkan potensi penghambatan MMP-9 tertinggi dengan nilai prediksi masing-masing sebesar 1; 1; 0,96; dan 0,95. Gen yang menjadi target potensial senyawa dalam merica hitam meliputi MMP-1, MMP-2, MMP-9, IL-6, IL-1 $\beta$ , TNF- $\alpha$ , dan MAPK1. Pengembangan lebih lanjut terhadap aktivitas *anti-aging* senyawa potensial merica hitam pada gen target perlu dilakukan melalui studi *in vitro* dan *in vivo*.

**Kata kunci:** penuaan kulit, MMP-9, merica hitam, sel fibroblas, bioinformatika

## ABSTRACT

Skin aging is mainly caused by ultraviolet (UV) rays causing loss of skin integrity. UV light causes over-expression of skin aging markers, one of them is matrix metalloproteinase 9 (MMP-9). It is an extracellular matrix degrading enzyme. Black pepper has benefit as an antioxidant, anti-inflammatory, and anti-senescence. This study aims to explore the potential of black pepper as an agent to prevent skin aging of fibroblast cells caused by UV light with MMP-9 as the target and the other one involved. Meta-analysis studies of bioinformatics and machine learning analysis were carried out through online databases and the use of software. The effect of UV light on the pathophysiology of skin aging was obtained through a literature search. MMP-9 expression levels were obtained through The Human Protein Atlas database. Aging-related target genes in fibroblast cells were obtained through the Genecards database. The metabolomic profile of black pepper was obtained through the CMAUP database. Potential inhibitors of black pepper compounds against MMP-9 were obtained through KNIME software and ChEMBL database. The potential target genes of black pepper were obtained through slices of target genes from the Genecards database and literature studies. The role of MMP-9 and related target genes was obtained through literature study and KEGG pathway database. The results of this study showed that UV light increased the expression level of MMP-9. Four black pepper compounds, namely pinocembrin, piplartin, piperine and  $\beta$ -caryophyllene, showed the highest MMP-9 inhibitory potential with predictive values of 1; 1; 0.96; and 0.95. Genes that are potential targets for compounds in black pepper include MMP-1, MMP-2, MMP-9, IL-6, IL-1 $\beta$ , TNF- $\alpha$ , and MAPK1. Further development of the anti-aging activity of potential black pepper compounds on target genes needs to be carried out through in vitro and in vivo studies.

**Keywords:** skin aging, MMP-9, black pepper, fibroblast cells, bioinformatics