INTISARI

Salah satu penyebab *brain disorder* seperti penyakit neurodegeneratif ialah peningkatan akivitas dan jumlah HDAC2. HDAC2 merupakan enzim yang mengkatalisis pelepasan gugus asetil pada protein histon sehingga menghambat ekspresi gen terkait neurogenesis. Penghambatan HDAC diketahui mampu memperbaiki neurodegenerasi dan meningkatkan ekspresi gen yang diatur asetilasinya. Kurkumin dilaporkan menghambat HDAC Kelas I secara *in vitro* yang berdampak pada peningkatan asetilasi H4. Studi *in vivo* kurkumin dan PGV-0 dilaporkan mampu meningkatkan gen terkait memori (*TrkB*) yang memberi usulan terkait *Bdnf* sebagai gen yang berperan dalam persinyalan terkait neurogenesis. SAHA sebagai HDACi mampu meningkatkan asetilasi H3 dan H4 *cortex* yang memicu diferensiasi neuron yang ditandai dengan peningkatan *β-III tubulin*. Adapun turunan kurkumin dan analognya memiliki kemiripan struktur dengan kurkumin. Nampaknya, senyawa kurkumin, turunan, dan analognya berpotensi mentarget HDAC pada *brain disorder*, khususnya *Hdac2* serta berimplikasi terhadap *Bdnf* dan gen terkait neurogenesis (*β-III tubulin*). Penelitian ini bertujuan untuk menelusuri secara kritis dalam *narrative review* tentang potensi beserta analisis struktural kurkumin, turunannya (demetoksikurkumin, CNB-001), dan analognya (PGV-0) sebagai kandidat agen terapi *brain disorder* terhadap ekspresi *Hdac2* serta implikasinya terhadap ekspresi gen terkait neurogenesis (*β-III tubulin*) dan *Bdnf*.

Database pencari artikel menggunakan Pubmed, ScienceDirect, dan Google Scholar. Cara seleksi artikel yang digunakan meliputi skrining judul, abstrak, dan isi artikel yang sesuai dengan kata kunci dan kriteria inklusi serta eksklusi yang ditetapkan, kemudian data diekstraksi, lalu dituangkan dalam *narrative review*.

Hasil studi menunjukkan kurkumin, demetoksikurkumin, CNB-001, dan PGV-0 berpotensi menghambat ekspresi *Hdac2* dan aktivitas HDAC2 melalui pendekatannya dalam perbaikan fungsi otak pada model *brain disorder* dan berpotensi meningkatkan ekspresi *Bdnf* serta *β-III tubulin*. Adapun penghambatan HDAC2 oleh senyawa tersebut memiliki pendekatan model farmakofor berupa ZBG, gugus *linker*, dan gugus *capping*.

Kata Kunci : Kurkumin, *brain disorder*, *Hdac2*, *Bdnf*, *β-III Tubulin*

ABSTRACT

One cause of brain disorders such as neurodegenerative diseases is an increase in activity and the amount of HDAC2. HDAC2 is an enzyme to remove acetyl groups in histone proteins thereby inhibiting the expression of genes related to neurogenesis. HDAC inhibition is known to improve neurodegenerative and increase the expression of genes which is regulated by and genes related to neurogenesis. Curcumin is reported to inhibit HDAC Class I in vitro which has impact on increasing H4 acetylation. In vivo studies of curcumin and PGV-0 are reported to increase memory-related genes (*TrkB*) which give recommendations regarding *Bdnf* as genes that play a role in signaling related to neurogenesis. SAHA as HDACi can increase the acetylation of H3 and H4 cortex which triggers neuron differentiation which is characterized by an increase in *β-III tubulin*. Curcumin, its derivatives, and its analog have similar structures with curcumin. Apparently, curcumin, its derivatives, and its analog have the potential to target HDAC in brain disorders, especially *Hdac2* and have implications for *Bdnf* and genes related to neurogenesis (*β-III tubulin*). This study aims to explore critically in a narrative review on the structural analysis of curcumin, its derivatives (demethoxycurcumin, CNB-001), and its analog (PGV-0) as candidates for brain disorder therapy agents for *Hdac2* expression and their implications for gene expression related to neurogenesis (*β-III tubulin*) and *Bdnf*.

The article search database uses Pubmed, ScienceDirect, and Google Scholar. The method of article selection is screening titles, abstracts, and article content in accordance with the keywords and inclusion and exclusion criteria set, then the data is extracted, then poured in a narrative review.

The results of this study show that curcumin, demethoxycurcumin, CNB-001, and PGV-0 potentially inhibit *Hdac2* expression and HDAC2 activity through their approach in improving brain function on brain disorder models and potentially increase *Bdnf* and *β-III tubulin* expression. The inhibition of HDAC2 by these compounds has a pharmacophore model approach in the form of ZBG, linker groups, and capping groups.

Keywords : Kurkumin, *brain disorder*, *Hdac2*, *Bdnf*, *β-III Tubulin*