

## ABSTRAK

### MEKANISME POLIFENOL TERHADAP REGULASI GEN *CIRCADIAN CLOCK* PADA KANKER PAYUDARA: *A NARRATIVE REVIEW*

**Latar Belakang:** Kanker payudara merupakan penyebab utama morbiditas dan mortalitas pada perempuan di seluruh dunia. Gangguan ritme *circadian* diketahui berperan dalam patogenesis dan progresivitas kanker payudara melalui disrupsi regulasi siklus sel, metabolisme, dan respons stres seluler. Polifenol sebagai senyawa bioaktif alami dilaporkan memiliki kemampuan memodulasi sistem *circadian clock*, namun mekanisme keterkaitannya dengan efek seluler pada kanker payudara masih belum dipahami secara komprehensif. **Tujuan:** Menelaah mekanisme polifenol dalam meregulasi gen *circadian clock* serta kaitannya dengan efek antikanker, antimetastatik, dan kemopreventif pada kanker payudara. **Metode:** Penelitian ini merupakan *narrative review* dengan penelusuran literatur pada basis data PubMed, Scopus, dan Web of Science menggunakan kata kunci terkait polifenol, *circadian clock*, dan kanker payudara. Artikel penelitian *in vitro* dan *in vivo* yang relevan dianalisis secara naratif. **Hasil:** Polifenol seperti nobiletin, quercetin, dan resveratrol dilaporkan memodulasi gen *circadian* utama, terutama PER2, BMAL1, dan reseptor inti ROR $\alpha/\gamma$ . Modulasi ini berasosiasi dengan penurunan proliferasi sel, inhibisi metastasis, induksi apoptosis, serta efek kemopreventif pada model kanker payudara. **Kesimpulan:** Polifenol berpotensi berperan sebagai modulator sistem *circadian clock* yang berasosiasi dengan pengendalian perilaku sel kanker payudara, sehingga memiliki prospek sebagai agen pendukung dalam strategi pencegahan dan terapi kanker payudara.

**Kata Kunci:** polifenol, *circadian clock*, kanker payudara

## **ABSTRACT**

### **MECHANISM OF POLYPHENOLS IN REGULATING CIRCADIAN CLOCK GENES IN BREAST CANCER: A NARRATIVE REVIEW**

**Background:** Breast cancer is the leading cause of morbidity and mortality in women worldwide. Circadian rhythm disorders are known to play a role in the pathogenesis and progression of breast cancer through disruption of cell cycle regulation, metabolism, and cellular stress responses. Polyphenols, as natural bioactive compounds, have been reported to have the ability to modulate the circadian clock system, but the mechanism of their association with cellular effects on breast cancer is not yet fully understood. **Objective:** To examine the mechanism of polyphenols in regulating circadian clock genes and their association with anticancer, antimetastatic, and chemopreventive effects in breast cancer. **Methods:** This study is a narrative review with literature searches on PubMed, Scopus, and Web of Science databases using keywords related to polyphenols, circadian clock, and breast cancer. Relevant *in vitro* and *in vivo* research articles were analyzed narratively. **Results:** Polyphenols such as nobiletin, quercetin, and resveratrol were reported to modulate key circadian genes, particularly PER2, BMAL1, and nuclear receptors ROR $\alpha$ / $\gamma$ . This modulation was associated with decreased cell proliferation, inhibition of metastasis, induction of apoptosis, and chemopreventive effects in breast cancer models. **Conclusion:** Polyphenols have the potential to act as modulators of the circadian clock system associated with the control of breast cancer cell behavior, thus offering prospects as supportive agents in breast cancer prevention and treatment strategies.

**Keywords:** polyphenols, circadian clock, breast cancer