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Ginsenosides as selective glucocorticoid drugs: agonists, antagonists, and prodrugs

Halima, M.

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Propositions

Accompanying the dissertation

Ginsenosides as selective glucocorticoid drugs: agonists, antagonists, and prodrugs

1. Non-glycosylated ginsenosides act as selective glucocorticoid receptor agonists, and glycosylation increases their selectivity of action (This thesis, Chapters 3, 5-7).
2. Due to their low binding affinity to the glucocorticoid receptor, ginsenosides are not appropriate for use as anti-inflammatory drugs in clinical settings, but their remarkably selective activation of this receptor renders them highly valuable as research tools (This thesis, Chapters 3, 5-7).
3. Ginsenoside Rg1 binds to the glucocorticoid receptor without activating it under basal conditions, but selectively activates it in inflamed tissues, making it a selective antagonist of the receptor (This thesis, Chapter 5).
4. Glycosylation of glucocorticoids transforms them into prodrugs that are converted into active compounds specifically in inflamed tissue, owing to the locally increased activity of the enzyme glucosylceramidase beta 2 (GBA2) (This thesis, Chapter 6).
5. Full glucocorticoid receptor activity, including both transrepression and transactivation, is essential to adequately control inflammation with glucocorticoid drugs (Vandevyver et al., 2014; Strickland et al., 2022).
6. Even though anti-inflammatory medication has been crucial for treating patients with acute COVID-19, pro-inflammatory therapy may be beneficial for individuals with long COVID-19 syndrome (Kovarik et al., 2023).
7. The activity of the enzyme glucosylceramidase beta 2 (GBA2) plays a significant role in the inflammatory response (Loberto et al., 2014; Schiumarini et al., 2017).
8. Exploring the pharmacological effects of naturally occurring compounds derived from plants paves the way for the development of innovative medications.
9. Luck comes from intelligence and hard work.
10. You have to accept challenges and take risks because life begins at the end of your comfort zone.

Mahmoud Halima, Leiden, 13 June 2023