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Multifaceted Evaluation of Anticancer, Antibacterial, Antifungal, and Anti-Candida Properties of Novel Cannabinoid Receptor 2 (CB2R) Ligands: An Integrated *In Vitro* and *In Silico* Analysis

Hussah N Albahlal [1], Danah Aloumi [1], Sarah Bin Saqyah [1], Arwa Alsubait [2], Jehan Alamre [2], Afrah E Mohammed [3], Reham M Aldahasi [3] , Nada Alharbi [3], Mohammed Alrashed [1] , Sahar S. Alghamdi [1,2]*

[1] Department of Pharmaceutical Sciences, College of Pharmacy, King Saud bin Abdulaziz University for Health Sciences, Riyadh 11451, Saudi Arabia.
[2] King Abdullah International Medical Research Center (KAIMRC), Riyadh 11481, Saudi Arabia.
[3] College of Pharmacy, Princess Nourah bint Abdulrahman University, Riyadh 11671, Saudi Arabia.

INTRODUCTION & AIM

- Cancer and microbial infections, encompassing fungal infections such as Candida and bacterial infections, constitute significant global health threats with considerable public health impact (1).
- Cannabinoids 2 Receptor (CB2R) ligands represent a diverse class of medications, including agonists, antagonists, and inverse agonists, with limited studies on their indications (2).
- The study aims to investigate the CB2R agonist (CB65) and inverse agonist (JTE907) for various applications, including anticancer, antibacterial, antifungal, and anti-Candida effects, using *in vitro* and *in silico* approaches.

METHOD

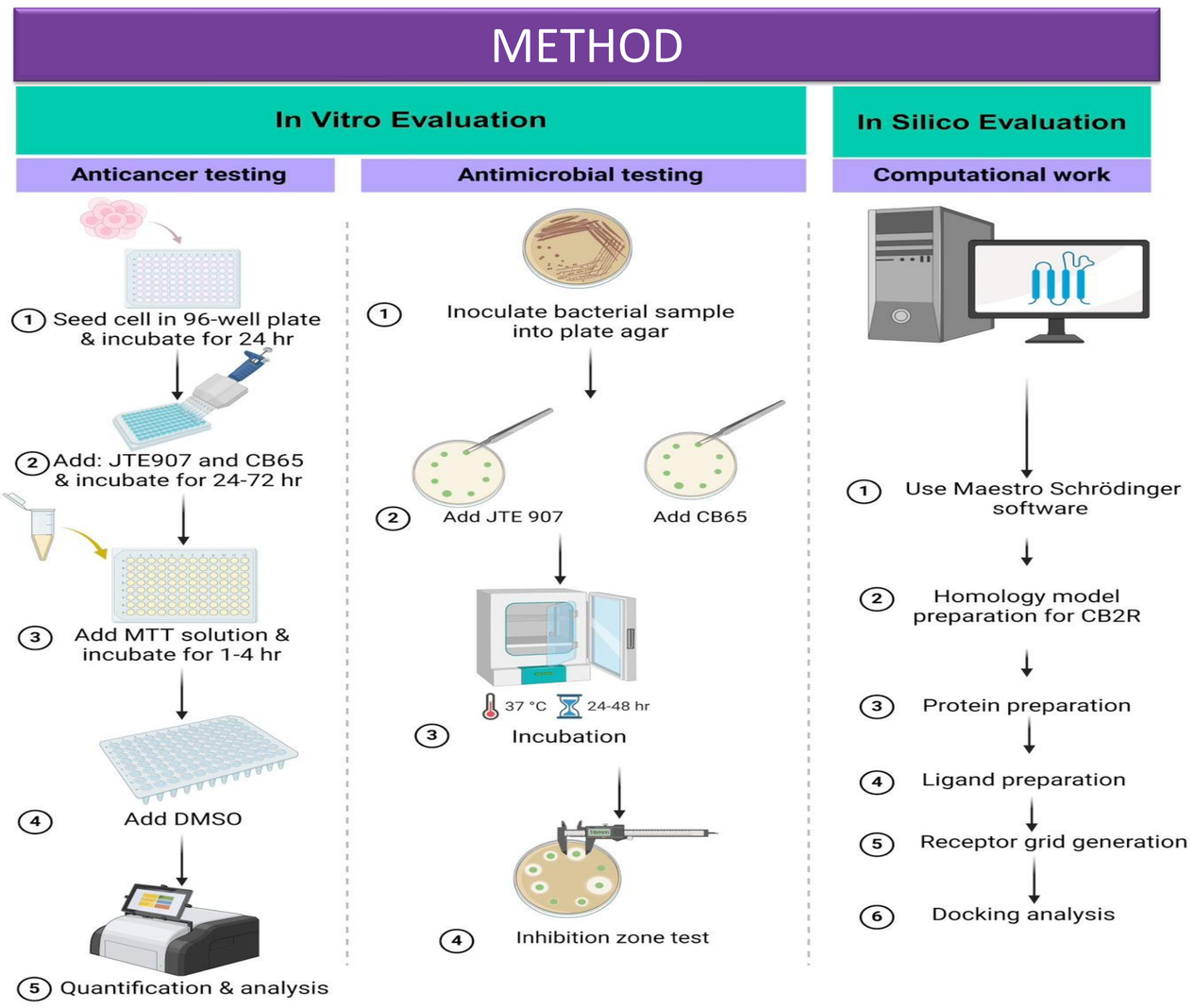

Figure.1: Experimental protocol.

RESULTS & DISCUSSION

- *In Vitro* Studies -

A) Anticancer Testing

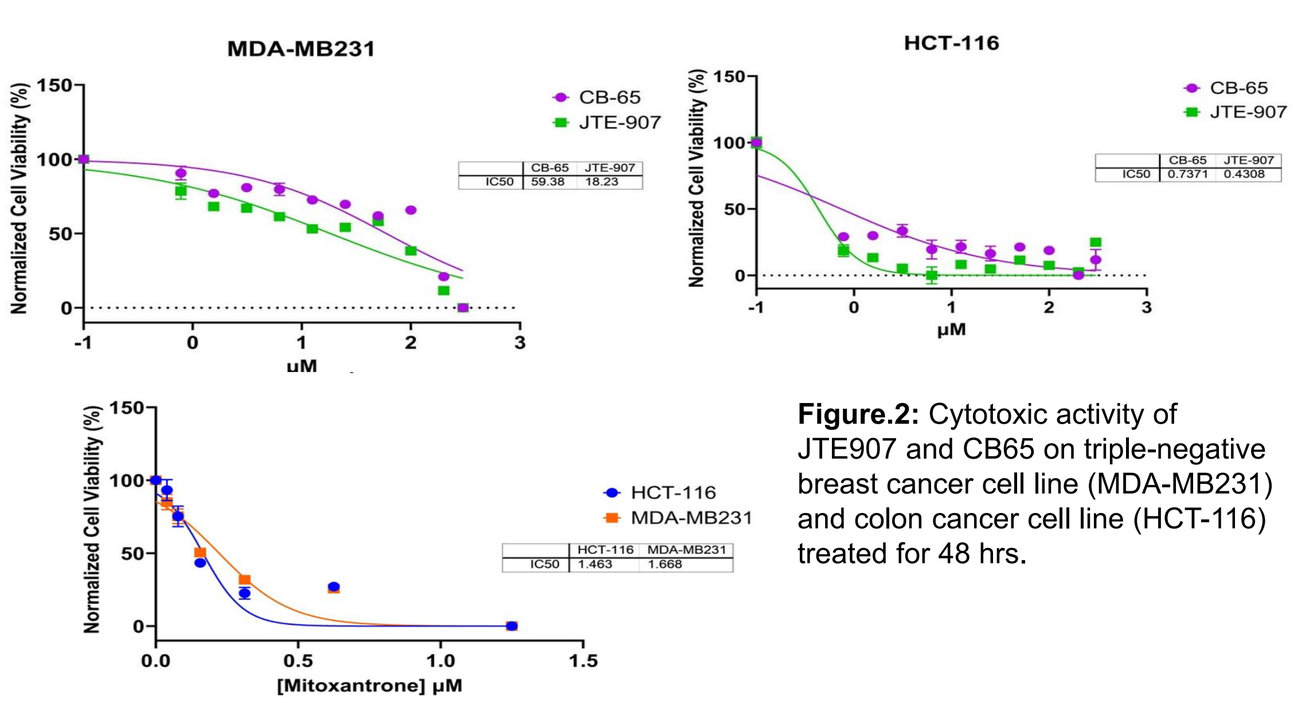

Figure.2: Cytotoxic activity of JTE907 and CB65 on triple-negative breast cancer cell line (MDA-MB231) and colon cancer cell line (HCT-116) treated for 48 hrs.

B) Antimicrobial Testing

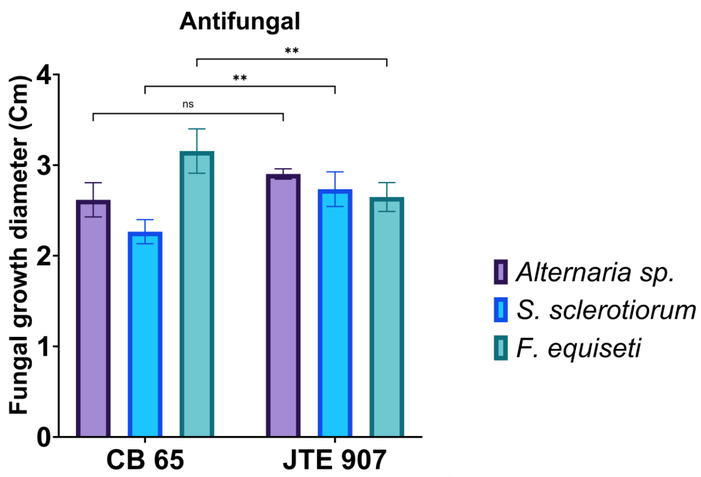

Figure.3 : Summary of anti-fungal activity represented as fungal growth diameter of CB2R ligands (JTE907 and CB65) against filamentous fungi (Alternaria sp., S. sclerotiorum, F. equiseti). Tebuconazole (positive antifungal agent) at 10 ppm resulted in zero growth of all tested fungal species.

- *In Silico Studies* -

A) Homology Model

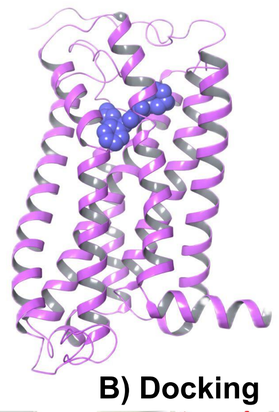

Figure.4: Homology model of CB2R. The surface model illustrates the overall shape and surface characteristics of the binding site, highlighting the interaction regions.

B) Docking

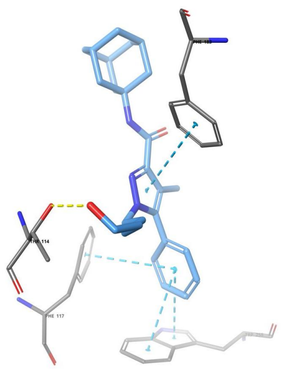

Figure.5: Binding Model of native ligand with CB2R. The binding model shows the detailed interactions between the native ligand within the CB2R binding site.

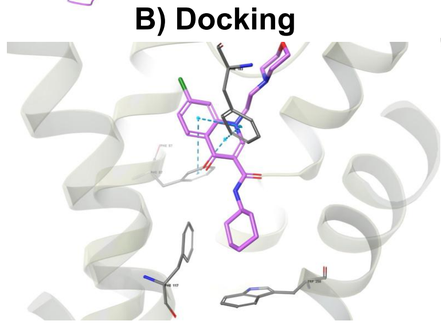

Figure.6: Binding Model of (CB65) with CB2R. The binding model shows the detailed interactions between CB65 and the key residues within the CB2R binding site.

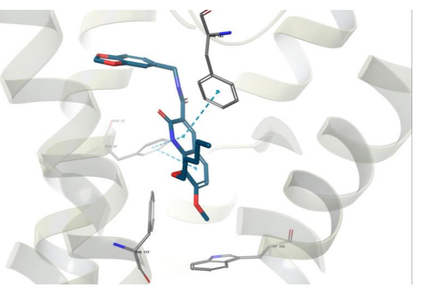

Figure.7: Binding Model of (JTE907) with CB2R. The binding model shows the detailed interactions between JTE 907 and the key residues within the CB2R binding site.

Table.1: Docking scores of JTE907 , CB65, and native ligand with CB2R. The binding affinity was calculated with the Maestro software, indicating the potential strength and stability of the interaction between JTE907 , CB65 , and CB2R.

Compound	Docking Mode	Docking Score (kcal/mol)	Interacting Amino Acid
Native Ligand	SP	-10.8	TRP 258, TRP 194, PHE 117, THR 119
(ID:ZDG)	XP	-12.2	
JTE907	SP	-8.8	PHE 87, PHE 183
	XP	-9.4	PHE 117, TRP 258, PHE 183, THR 114
CB65	SP	-9.5	PHE 87, PHE 183
	XP	-10.8	PHE 117, TRP 258, PHE 183, THR 114

CONCLUSION

- Synthetic Cannabinoids (JTE907 and CB65) demonstrate potent cytotoxic activity against triple-negative breast cancer and colon cancer cell lines and significant antimicrobial activity against filamentous fungi. However, both CB2R ligands showed no anti microbial activity against Gram-negative bacteria (Escherichia coli and Klebsiella pneumoniae), Gram-positive bacteria (Staphylococcus aureus) and Candida species. Molecular docking studies with CB2R showed strong binding affinities for both agents , with involving key interactions with amino acids PHE87 and, TRP258. These results suggest that JTE907 and CB65 has promising lead molecule with potent anticancer and antifungal properties that warrants further investigation.

REFERENCES

1- de Martel, C., Georges, D., Bray, F., Ferlay, J., & Clifford, G. M. (2020). Global burden of cancer attributable to infections in 2018: a worldwide incidence analysis. The Lancet. Global health, 8(2), e180–e190. https://doi.org/10.1016/S2214-109X(19)30488-7

2- Smoum, R., Grether, U., Karsak, M., Vernall, A. J., Park, F., Hillard, C. J., & Pacher, P. (2022). Editorial: Therapeutic potential of the cannabinoid CB2 receptor. Frontiers in pharmacology, 13, 1039564. https://doi.org/10.3389/fphar.2022.1039564