Light-activated natural product extracts for Photodynamic Inactivation of Bacteria

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Background

Photodynamic Inactivation (PDI) is a light-triggered antimicrobial strategy that utilizes a photosensitizer (PS) that can be activated by specific wavelengths of light to generate of cytotoxic singlet oxygen and other reactive molecular species (RMS) for destroying unwanted and highly resistant bacteria pathogens. Many naturally occurring compounds in plants are produced as secondary metabolites and function as photosensitizers in complex defense mechanisms against pathogens and herbivores. Photosensitizers are classified based on their structure and chemical origin. Some examples of natural product photosensitizers include anthraquinones, coumarins, perylenequinones, benzofurans, and flavin derivatives; whereas synthetically derived PSs include porphyrins, phenothiazines, etc.

Objective

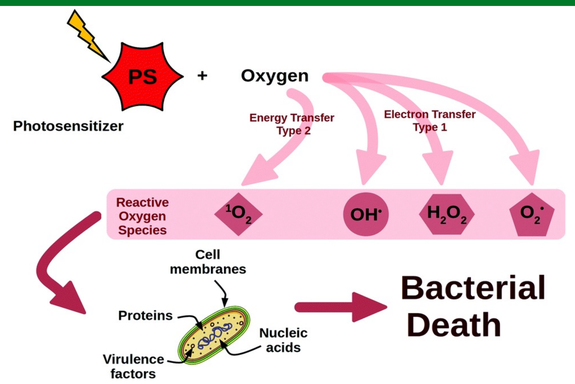
The emergence of antimicrobial resistance (AMR) against conventional antimicrobials presents a problem with a clear unmet need, leading to a search for alternative strategies. Our objective is to develop PSs that can produce an immediate burst of relatively nonspecific cytotoxic singlet oxygen and and other RMS to overcome AMR and that can selectively target highly resistant bacterial cells.

Natural product extracts

a. Japanese knotweed *(Reynoutria japonica)*
b. Turmeric root *(Curcuma longa)*
c. Aloe vera *(Aloe barbadensis miller)*
d. Rhubarb root *(Rheum rhabarbarum)*
e. Yellow dock *(Rumex crispus)*

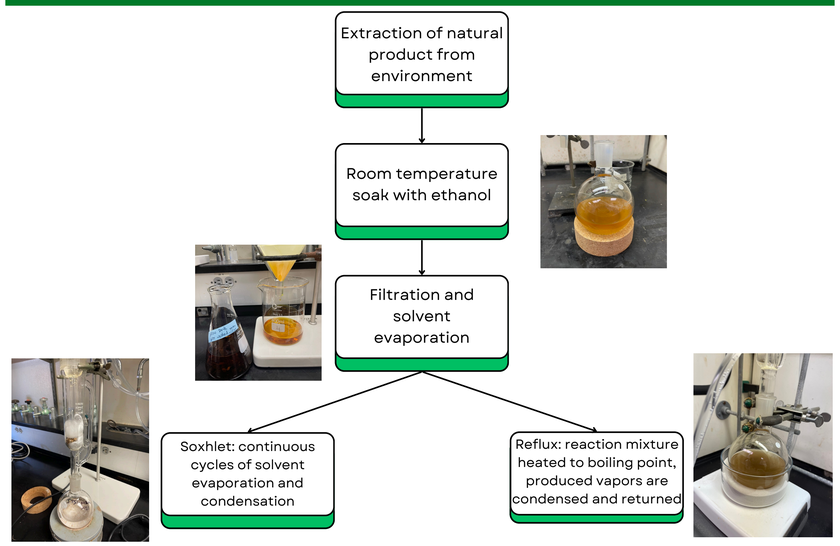
a. 
b. 
c. 
d. 
e. 

Photo-antimicrobial chemotherapy



Upon light activation, the PS can participate in type-I (electron transfer) or type-II (energy transfer) processes which lead to production of cytotoxic singlet oxygen and other RMS that can damage microbial cells, including AMR species, and lead to cell death.

Workflow



Results

Japanese knotweed

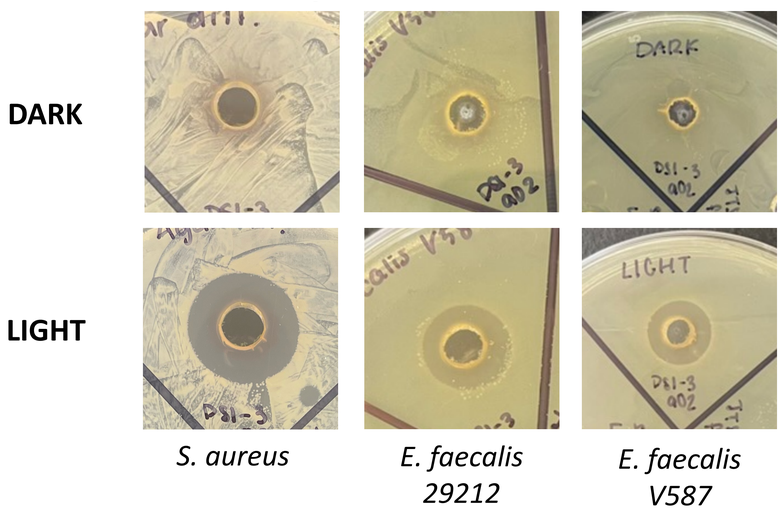


Table of inhibition zones (ZOIs)

ZOI (cm) / Extracts	*S. Aureus*	*E. faecalis 29212*	*E. faecalis V587*	*E. coli*	*A. baumannii*
Turmeric root chip (Soxhlet)	1.0	1.0	1.1	x	x
Turmeric root chip (reflux)	x	1.0	x	x	x
Yellow dock (washed)	1.5	1.4	1.3	x	x
Yellow dock (unwashed)	1.5	1.5	1.4	x	x
Japanese knotweed (Amazon)	1.6	1.4	1.3	x	x
Knotweed (Thera-Plantes)	1.6	1.5	1.4	x	x
Aloe vera leaf (reflux)	1.0	1.0	1.0	x	x
Rhubarb chip	1.5	1.3	1.5	x	x

Under DARK conditions no inhibition was observed; "x" refers to no measurable inhibition zone

Future studies

These results will be validated using more quantitative approaches such as minimum inhibitory concentration (MIC) assays to compare their antimicrobial and photo-antimicrobial properties across various bacterial species, including AMR strains. Bioassay-guided fractionation will be used to optimize the photocytotoxicities against the AMR strains for the lead natural product extracts.

Acknowledgements

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References

1. Arenas, Y. *Photodiagnosis and Photodyn. Ther*. **2013**, *10* (4),615-625.
2. Carmona, N.M. *Photochem. Photobiol. Sci.* **2020**, *19*, 445-461.
3. Ghorbani, J. *Laser Ther.* **2018**, *27* (4), 293-302.
4. Rajesh, S. *J Indian Soc Periodon*. **2011**, *15* (4), 323-327.
5. Monro, S. *Chemical Reviews* **2019**, *119* (2), 797-828.

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