Natural Product Extracts as Photosensitizers for the Photodynamic Inactivation of Bacteria

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Background

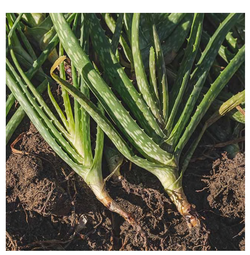
Photodynamic Inactivation (PDI) is a light-triggered antimicrobial strategy that utilizes a photosensitizer (PS) that can be activated by specific wavelengths of light to generate of cytotoxic singlet oxygen and other reactive molecular species (RMS) for destroying unwanted and highly virulent pathogens. 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 photosensitizers include various tetrapyrrolic structures and metal complexes.

Objective

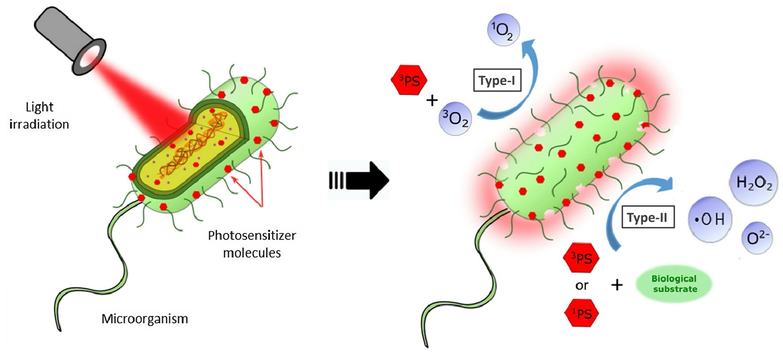
The emergence of antimicrobial resistance (AMR) to our most powerful drugs for treating infection presents a problem with a clear unmet need, leading to a search for alternative strategies. Our objective is to develop photosensitizers that can produce an immediate burst of relatively nonspecific cytotoxic singlet oxygen 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. 

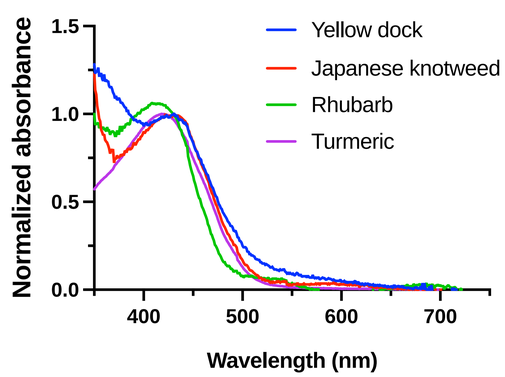
Photodynamic Inactivation



Upon light activation, the photosensitizer 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.

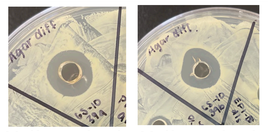
Workflow

UV-Vis Spectroscopy



Spectra were collected on samples dissolved in water at a concentration of 30 µg mL^{-1}. The extracts absorb light in the visible part of the spectrum (400-700 nm).

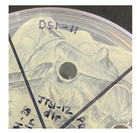
Results

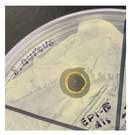

Yellow dock (washed)

Yellow dock (unwashed)


Japanese knotweed


Rhubarb root

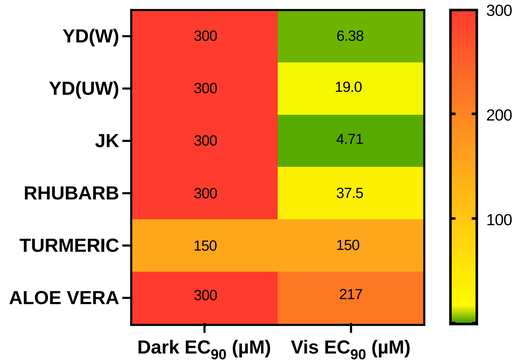

Turmeric root (reflux)


Turmeric root (soxhlet)


Aloe vera leaf

NP Extracts	ZOI (cm)
Yellow dock (washed)	1.5
Yellow dock (unwashed)	1.5
Japanese knotweed	1.6
Rhubarb root	1.5
Turmeric root (reflux)	0
Turmeric root (soxhlet)	1.0
Aloe vera leaf	1.0

Without light, no inhibition was observed; "0" refers to no measurable inhibition zone



Qualitative (agar diffusion) and quantitative (microbroth dilution) assays were used to evaluate the extracts' photobiological activities in *S. aureus* under dark and broadband visible light (fluence = 100 J cm^{-2} and irradiance = 28—35 mW cm^{-2}). EC_{90} is the concentration of compound required to reduce cell viability by 90%.

Future studies

Future MIC assays will compare antimicrobial and photo-antimicrobial properties of the most potent extracts across different bacterial species, including gram-negative and AMR strains.

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. Wang, Q. *J Colloid Interface Sci*. 2021, 584 (15), 539-550.
5. Monro, S. *Chemical Reviews* **2019**, *119* (2), 797-828.

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