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Vienna Doctoral School of Pharmaceutical, Nutritional and Sport Sciences

# Biopharmaceutical characterization of sanggenons from *Morus alba* root bark extracts: Can inhalation administration provide a therapeutic benefit in acute respiratory infections?


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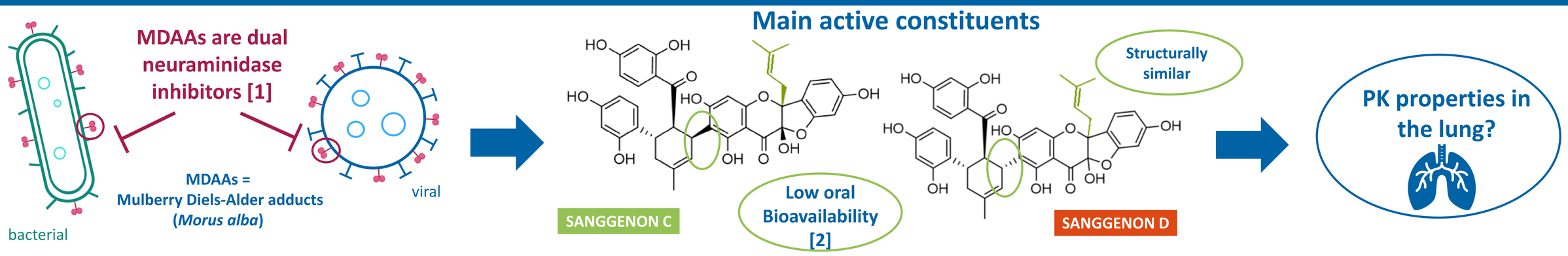
## BACKGROUND AND STUDY QUESTIONS




## EXPERIMENTAL AIMS

- Characterise pH-dependent solubility profiles of purified sanggenon C & D
  - Determine if extract components influence solubility
- Characterise cytotoxic concentration ranges
  - Determine if extract components influence cytotoxicity
- Characterise permeability behaviour
  - Determine if extract components influence permeability

## MATERIAL & METHODS

### SOLUBILITY

Preliminary solubility data was evaluated via a pH-dependent adapted and miniaturized version of the traditional shake-flask method. Compound concentrations were examined after 24h exposure in various buffers with pH values of 1.2, 4.5, 6.8 and 7.4. Investigated were solubility properties of sanggenon C and D and sanggenon C and D in form of the extract mixture.

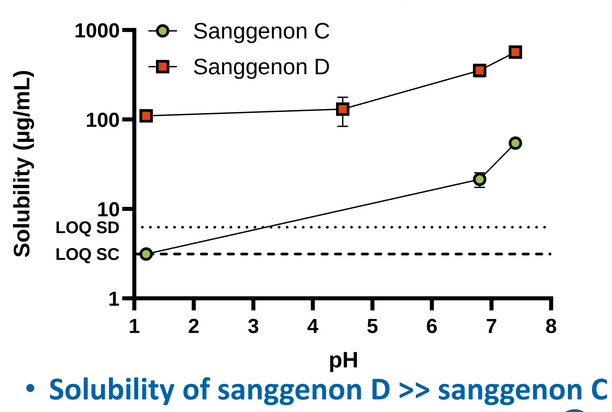
### CYTOTOXICITY

CC50 values of MDAA extracts (MA21 and MA60 [3]) and major constituents were assessed via MTT cytotoxicity assay. The Assay was conducted with Calu-3 cells, a human bronchial epithelial cells line with a 24h incubation period. Non-cytotoxic concentrations had to be evaluated for the conductance of following permeability studies. Reduction under 70% of viability was considered as non toxic.

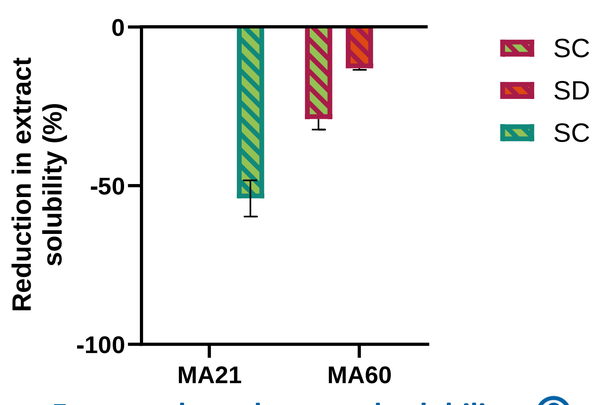
### PERMEABILITY

Calu-3 cells were seeded on inserts of transwell® plates and incubated until the cells formed an intact monolayer with tight junctions, which was verified by measuring TEER (Trans Epithelial Electrical Resistance) values.
Preliminary permeability assay was conducted with previous confirmed non-toxic concentrations of MDAAs extract MA5N.

## SOLUBILITY

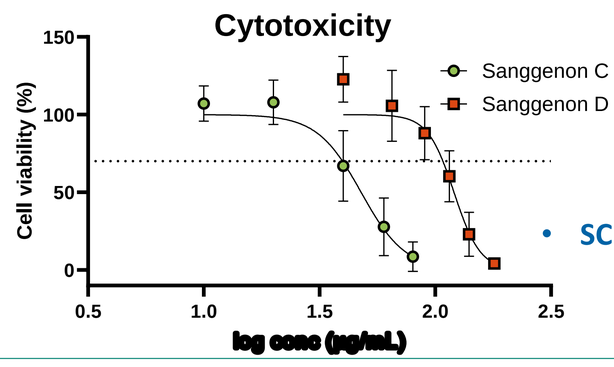



- Solubility of sanggenon D >> sanggenon C
- Unexpected pH-dependant solubility

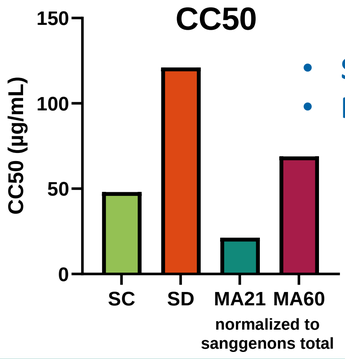



- Extracts show decreased solubility

## CYTOTOXICITY




- SC >> SD

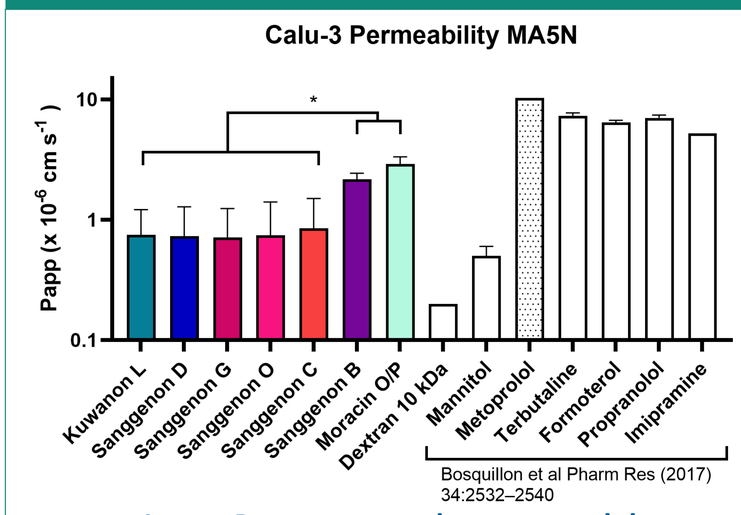



- SC < MA60 < SD
- MA21 << SC < SD

## CONCLUSION

- SC/ SD may have good lung bioavailability
- Similar molecules show very different solubility and cytotoxicity characteristics
- Results useful for formulation of inhaled sanggenons

## PERMEABILITY




Bosquillon et al Pharm Res (2017) 34:2532–2540

- Lower Papp compared to metoprolol
- Possible greater lung retention

## ACKNOWLEDGEMENTS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3. Langeder J. et al. (2023) J. Nat. Prod. 86 (1), 8-17.