Tech Session 2: Delivery Technologies in Consumer and Diversified Industrial Products(C&DP 1)

FATIMA ABID

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Advanced Delivery Science

University of South Australia

Antibiotic discovery for Resistant Acne Infections: Novel topical formulation development

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OUTLINE

- Introduction of model drug candidate ADS1
- Formulation development
- Physicochemical characterisation
- In vitro evaluation of encapsulated ADS1
- Conclusion and future directions
- Acknowledgement

ADS1

- Exhibit Antimicrobial properties
  - Anti-viral
  - Anti-fungal
  - Antibacterial
- Anticancer properties

REPOSITIONING

Cutibacterium acnes (C. acnes)

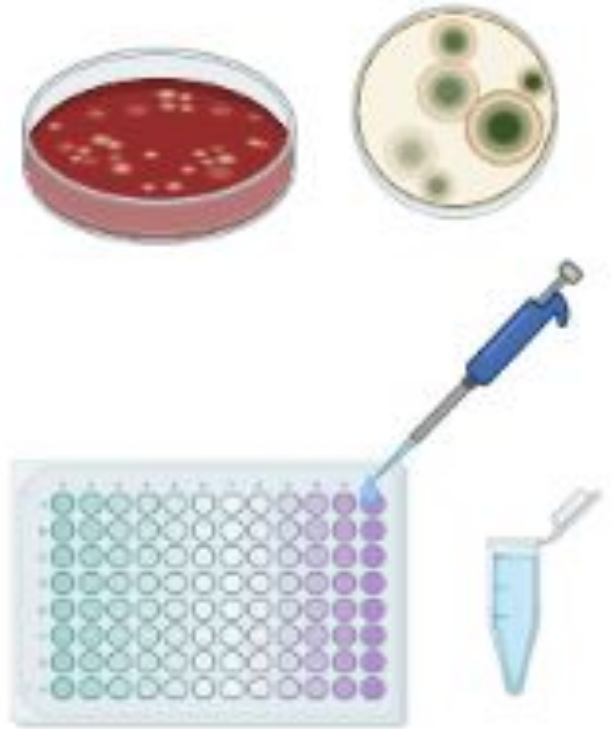
µg/mL	SDA321
MIC_{50}	0.031
MIC_{90}	> 0.062
MIC Range	≤ 0.008 – 0.062

Table 1. MIC_{50}, MIC_{90} and MIC range against *C. acnes* isolates

Staph aureus (S. aureus) and Staph epidermidis (S. epidermidis)

µg/mL	SDA321
S. aureus ATCC 29213	0.25
S. epidermidis ATCC 14990	0.25

Table 2. MIC range against *S. aureus* and *S.epidermidis* isolates



ANALYTICAL METHOD DEVELOPMENT

ADS1 Lacks chromophore

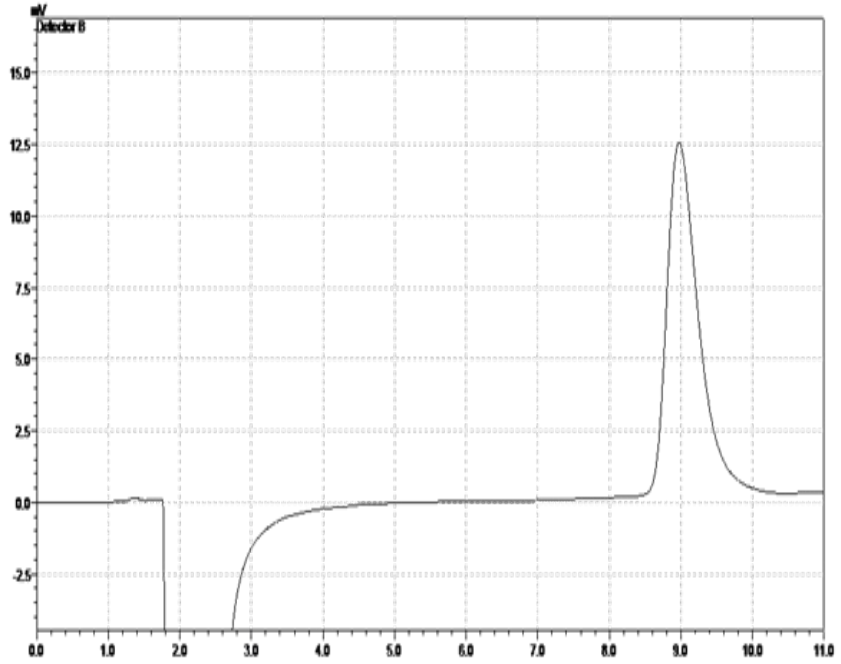


Fig 1: ADS1 Chromatogram (700 µg/mL)

Column	Eclipse Plus C18 (Agilent), 5µm, 4.6 x 150mm
Mobile Phase	Methanol: Water: Glacial Acetic Acid (92:8:1)
Flow rate	1 mL/min
Injection volume	50 µl
Temperature	30 C

Table 3: Method development parameters

Parameters	ADS1
Linearity range	200 – 900 µg/mL
Correlation coefficient (r)	1.0
Accuracy (Mean ± SD)	99.98 % ± 1.02
LOD	7.1 µg/ml
LOQ	21.50 µg/ml
Precision	< 2% (Pass)
Repeatability intermediate precision	RSD < 2% (Pass)
Robustness (Inj vol, temp)	RSD < 2% (Pass)
Systems suitability	Compliant

Table 4: Method validation parameters

GREENNESS EVALUATION

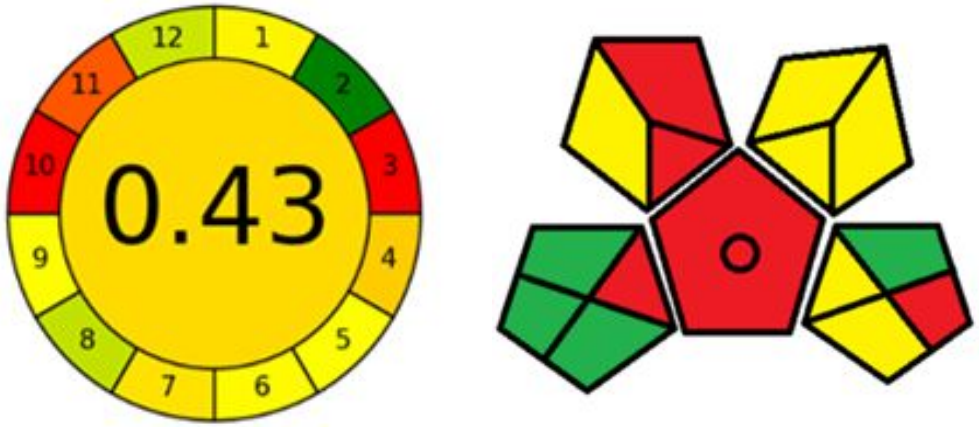


Fig 2: AGREE and GAPI pictogram of reported HPLC method

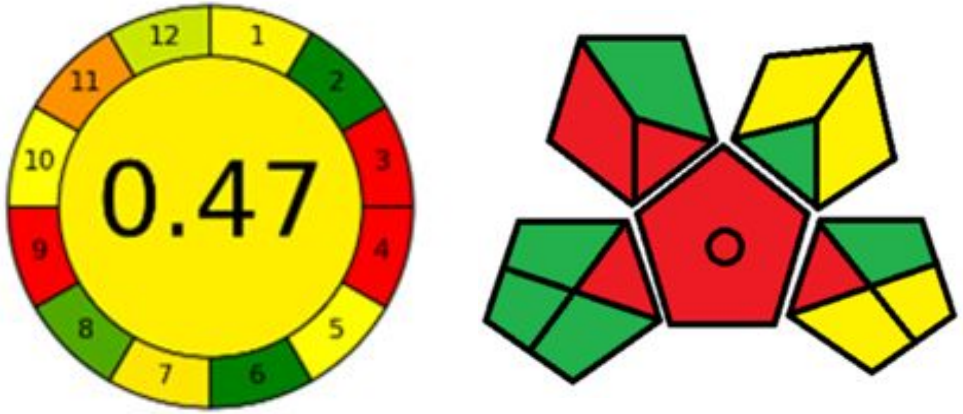


Fig 3: AGREE and GAPI pictogram of reported LCMS method

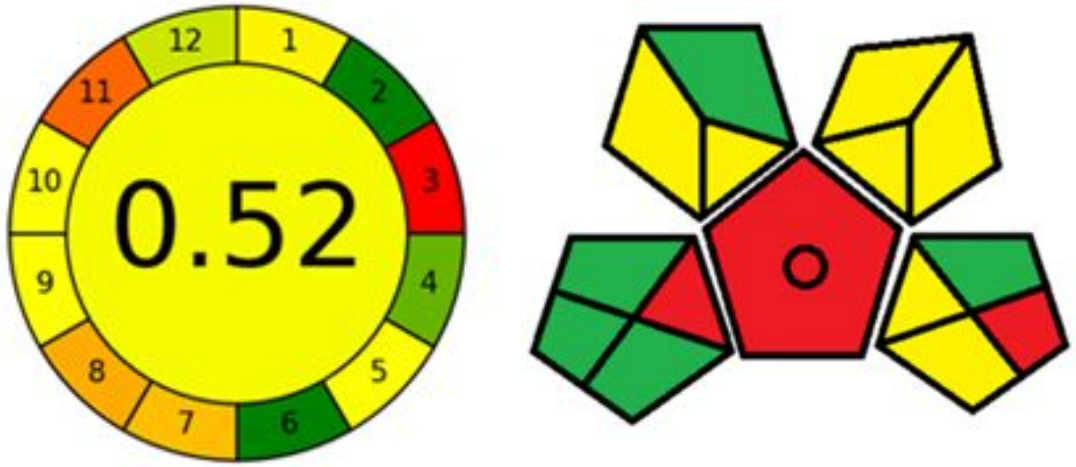


Fig 4: AGREE and GAPI pictogram of developed HPLC method

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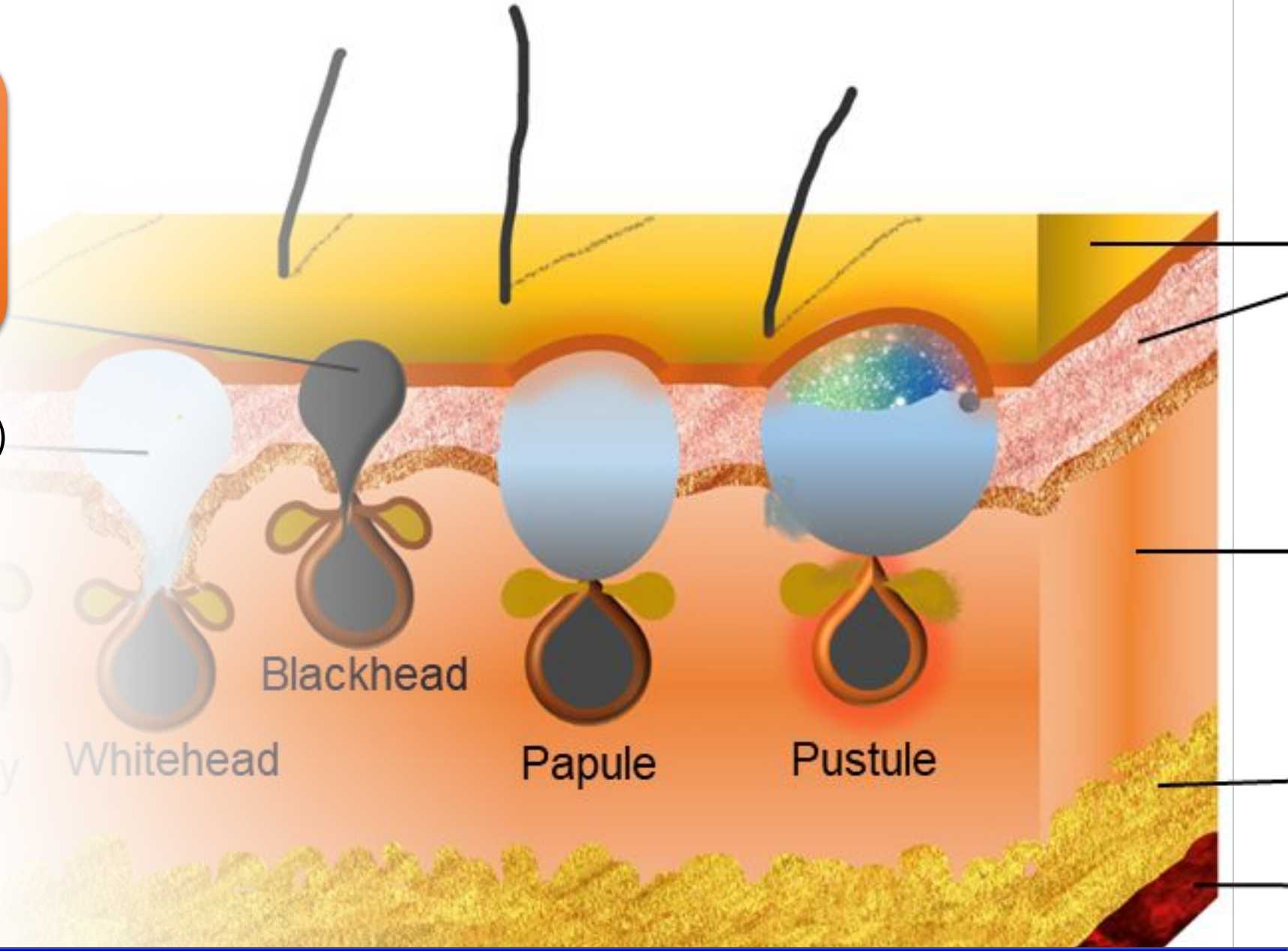
PIDG

CONSIDERATIONS FOR FORMULATION DEVELOPMENT

Poor aqueous solubility (<40 µg/mL)

Nano-sized carriers for efficient hair follicular delivery (SNMSD)



FORMULATIO N DEVELOPMEN T

- Polymer selection (Soluplus, HPMC (ASLG, ASMG)
- Drug: Polymer ratio (1:5)

F1	ADS1-Soluplus
F2	ADS1-HPMC ASLG
F3	ADS1-HPMC ASMG

SOLUBILITY ENHANCEMENT

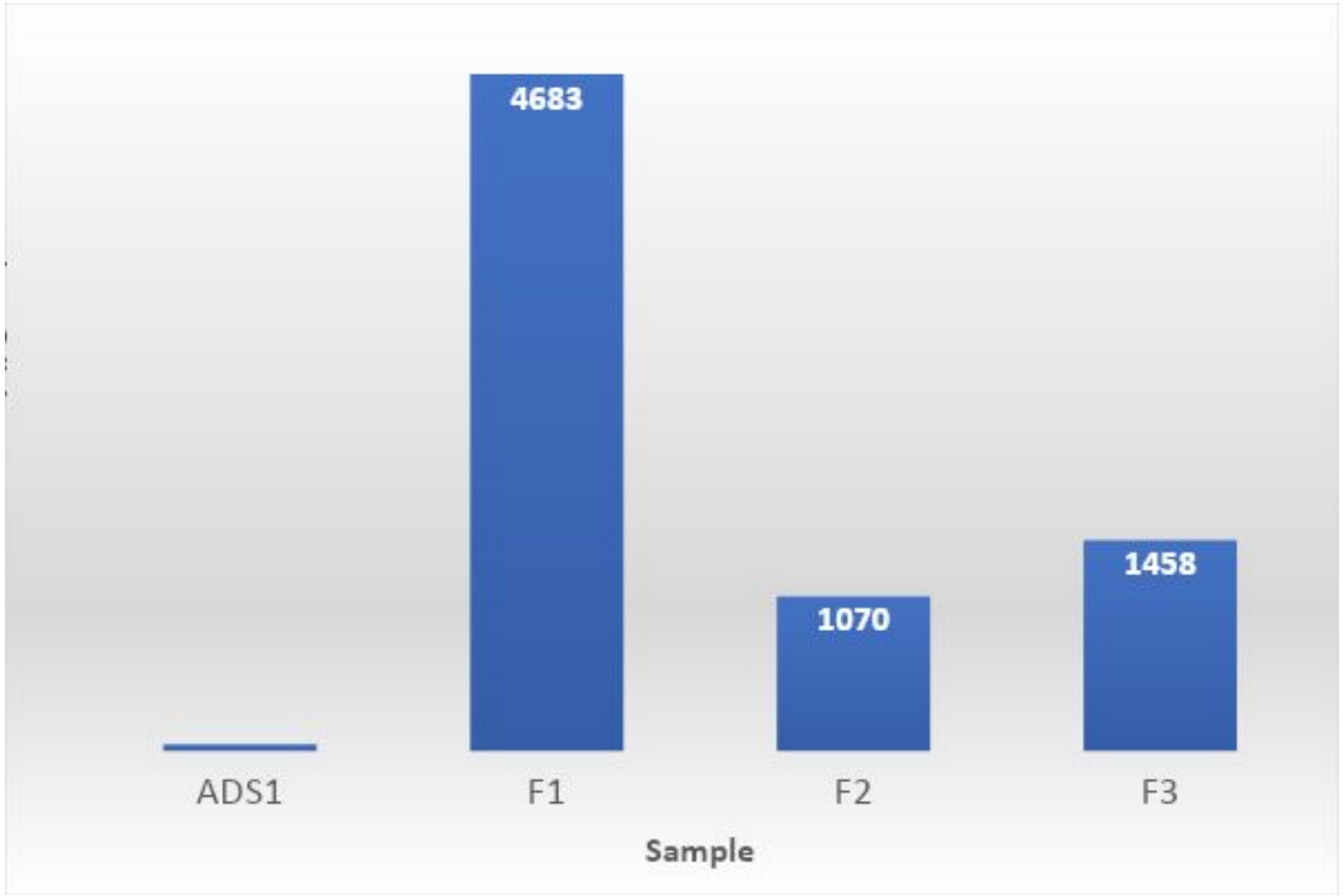


Fig 5. Solubility enhancement study

PHYSICOCHEMICAL CHARACTERISATION (1)

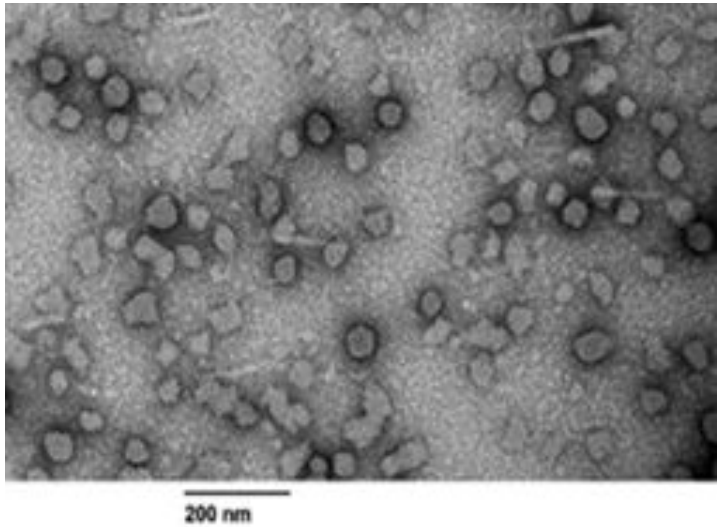


Fig 6. TEM image

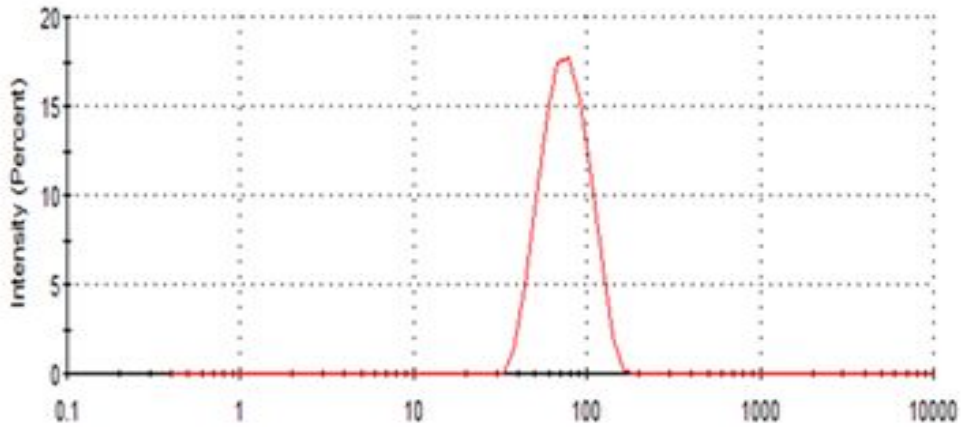


Fig 7. Particle size using DLS (71 nm)

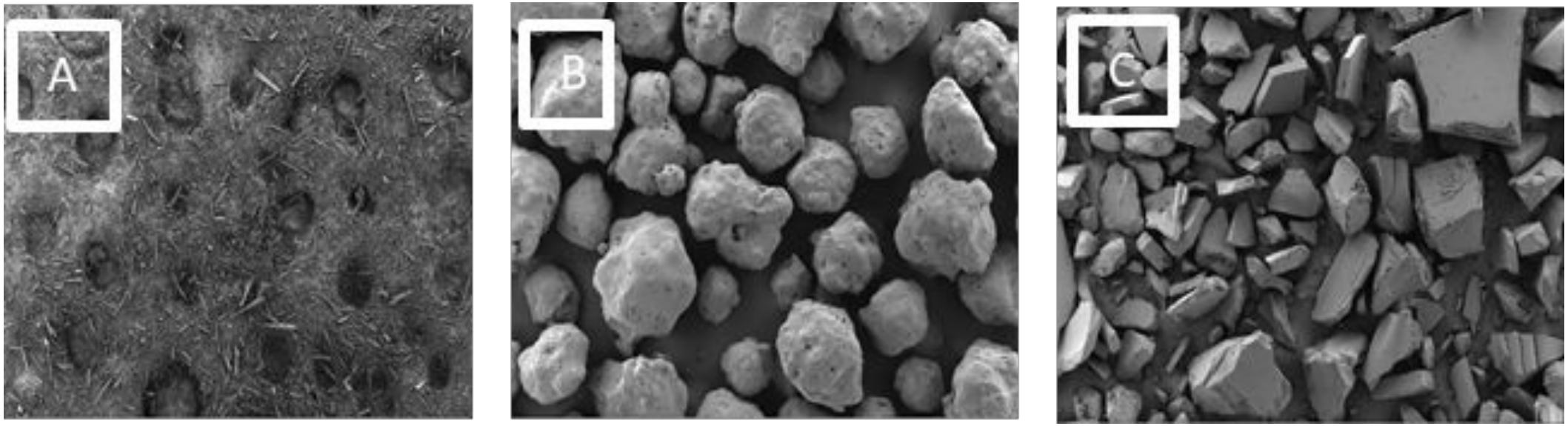


Fig 8. SEM study (A: ADS1; B: Soluplus; C: F1)

PHYSICOCHEMICAL CHARACTERISATION (2)

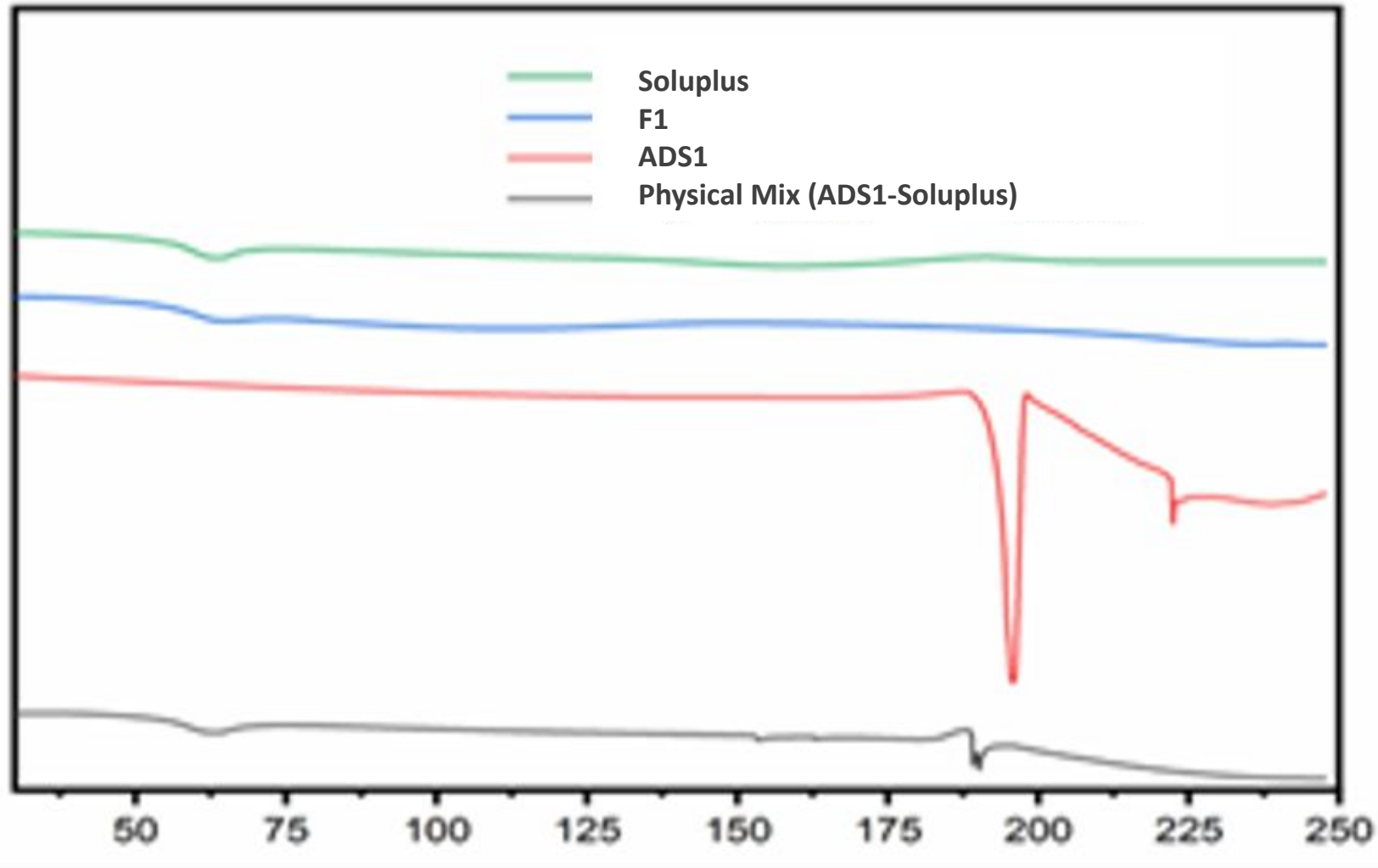
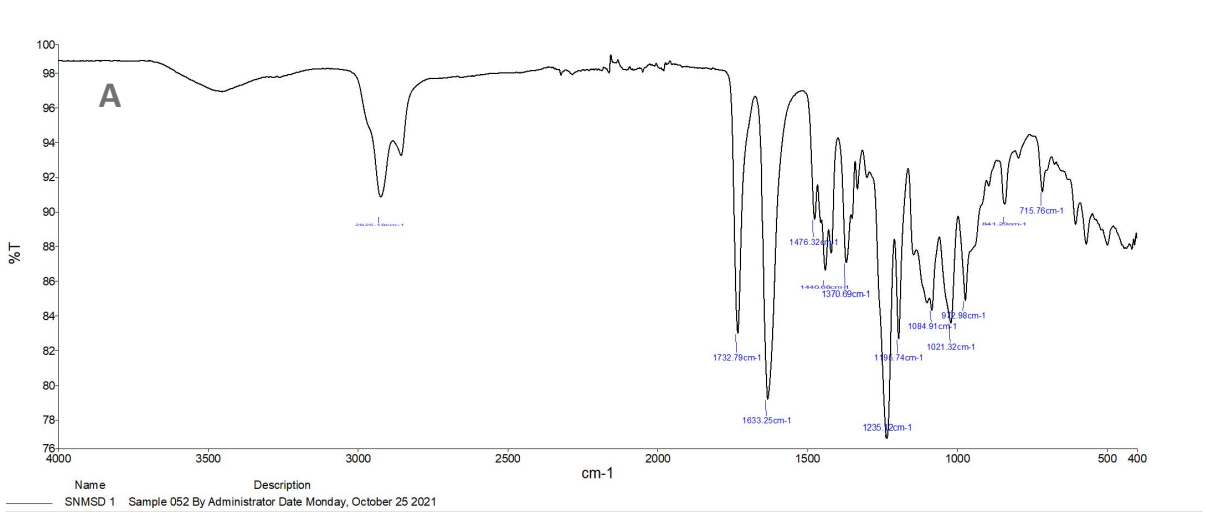
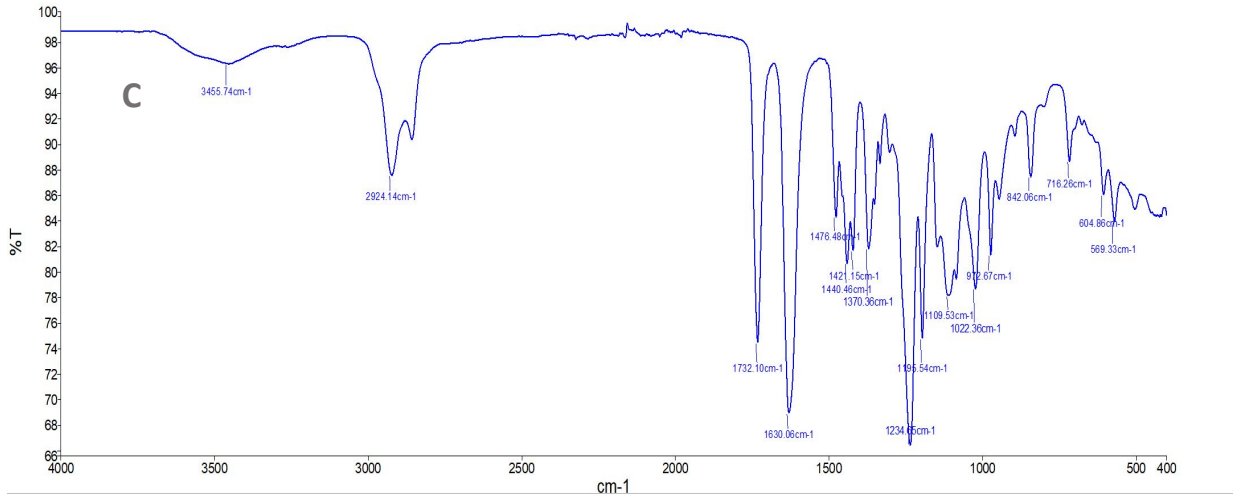
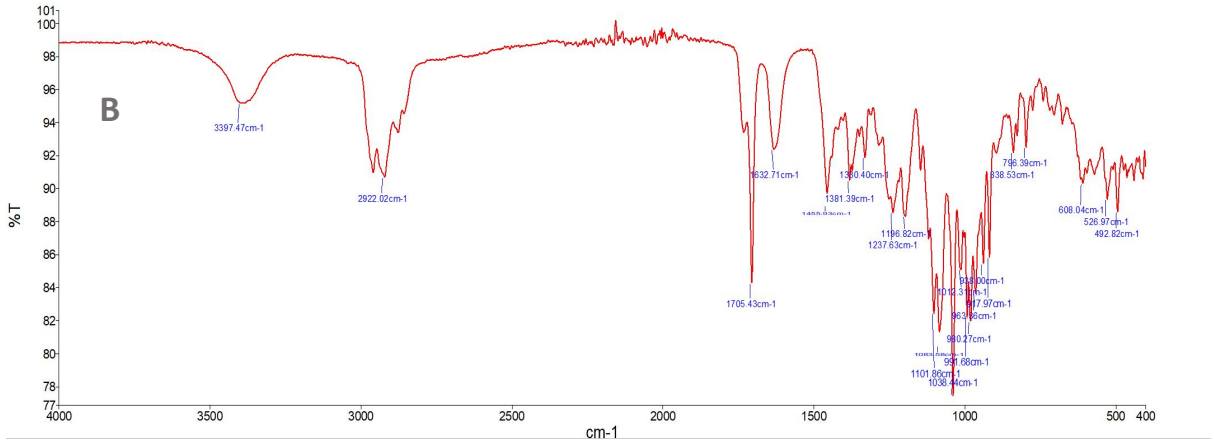


Fig 9. DSC study

PHYSICOCHEMICAL CHARACTERISATION (3)







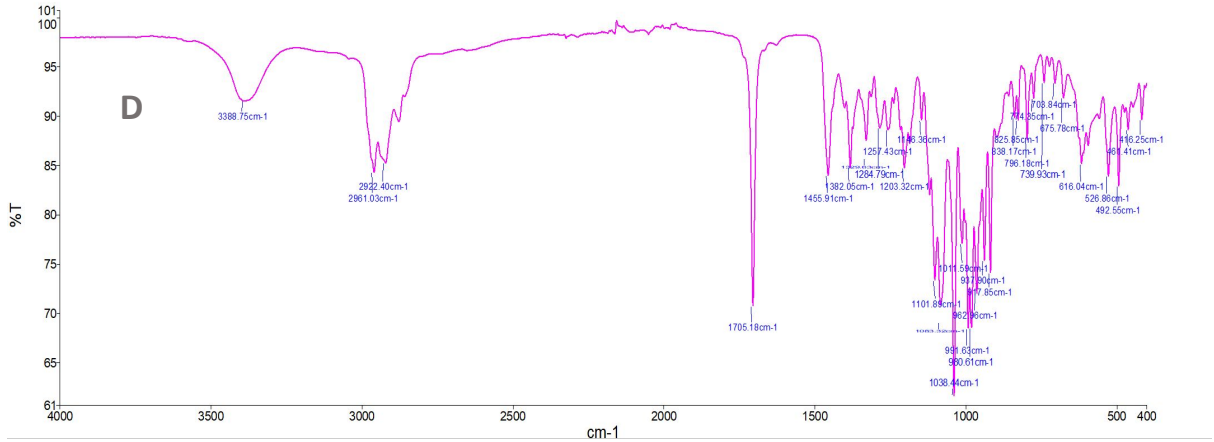
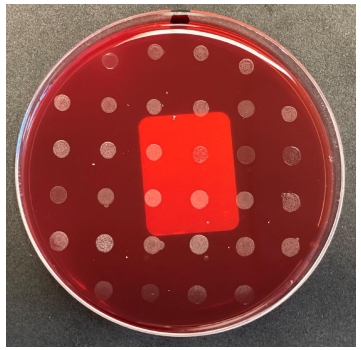
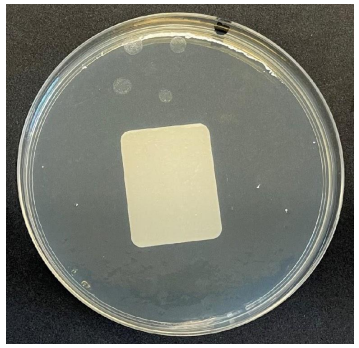


Fig 10. FTIR spectra (A: F1; B: Physical mix (ADS1-Soluplus); C: Soluplus; D: ADS1)

In vitro evaluation: Antibacterial activity and cell viability





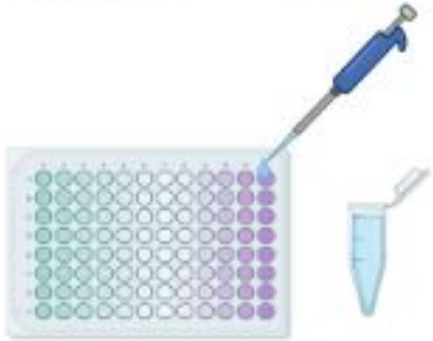
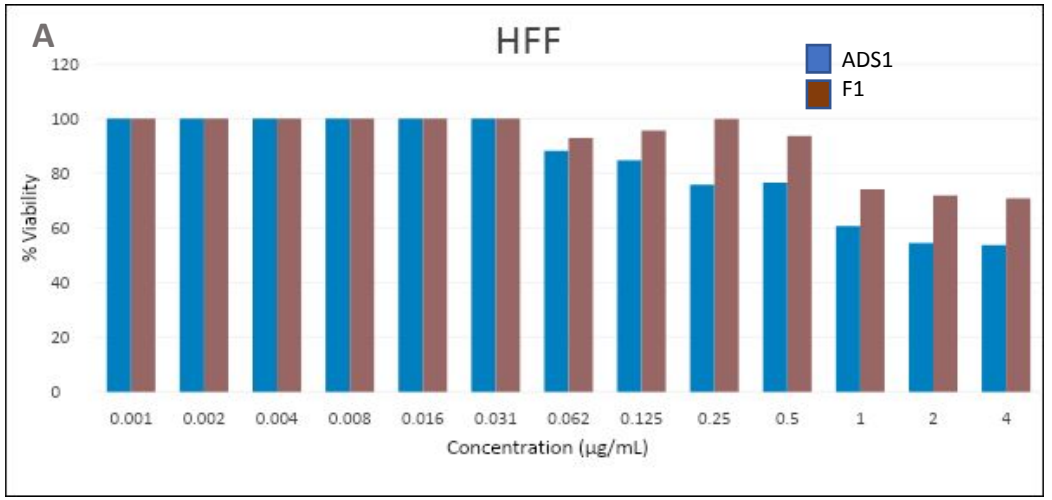


Table 5. MIC_{50}, MIC_{90} and MIC against *Cutibacterium acnes (C. acnes)*

µg/mL	ADS1	F1	F2	F3
MIC_{50}	0.031	0.031	0.062	0.062
MIC_{90}	> 0.062	> 0.062	> 0.062	> 0.062
MIC Range	≤ 0.008 – 0.062	≤ 0.008 – 0.062	≤ 0.008 – 0.062	≤ 0.008 – 0.062

Table 6. MIC range against *S. aureus* and *S. epidermidis*

µg/mL	ADS1	F1	F2	F3
S. aureus ATCC 29213	0.25	0.5	0.5	0.5
S. epidermidis ATCC 14990	0.25	0.5	0.5	0.5



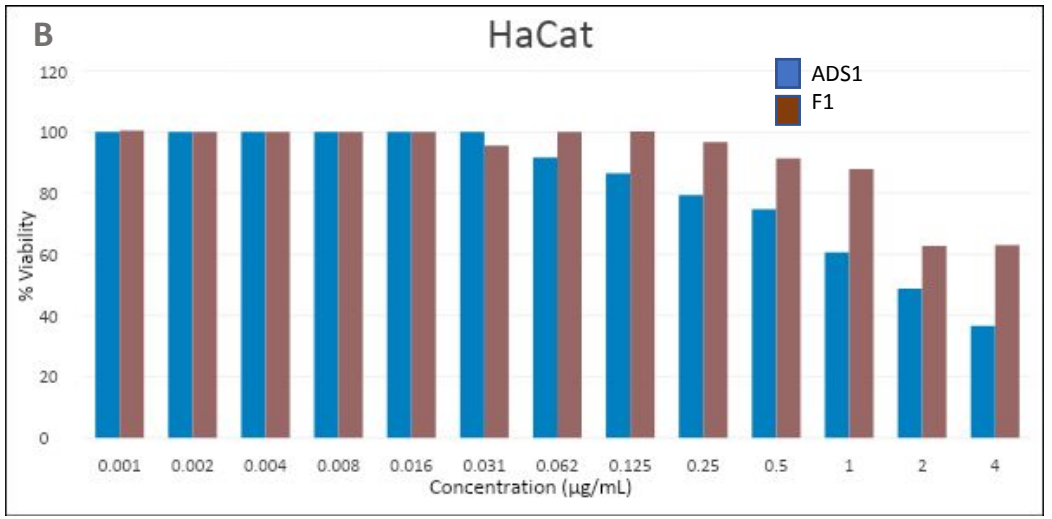


Fig 11. Percentage viability (A:HFF-1 cell line, B: HaCaT cell line)

CONCLUSION

- ADS1 is an effective antibacterial agent
- Self-nanomicellising solid dispersion presents a promising drug delivery technology for poorly water-soluble drugs
- Findings from in vitro evaluations in both bacterial and cellular systems warrant further studies with potential transfer into suitable in vivo models.
- Ongoing work: optimisation and further characterisation of ADS1-SNMSD incorporating transparent gel

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THANK YOU!

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