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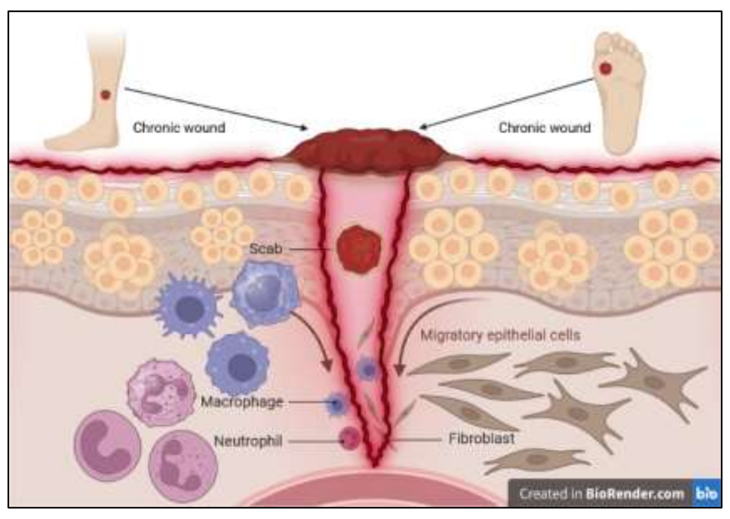
Citrus flavanone (naringenin)-infused transferosome based gel: Development, optimization, characterization with an exploration of diabetic wound healing potential through an integration of network pharmacology, *in vitro* and *in vivo* studies

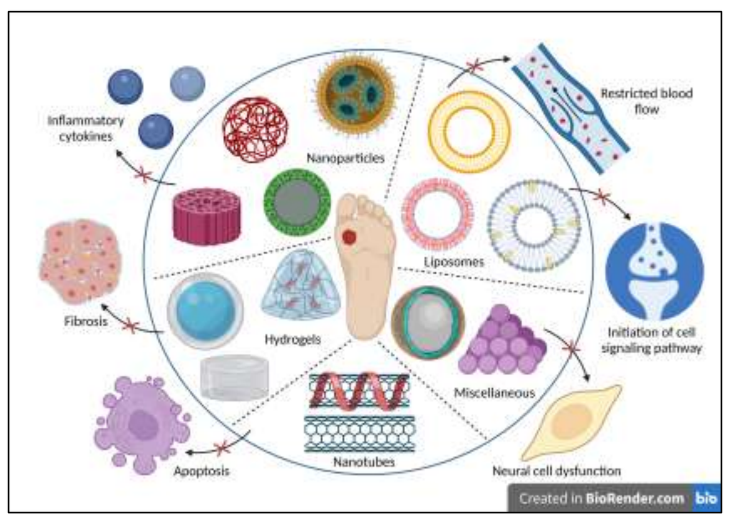
Ankit Chowdhury [1], **Bapi Gorain** [*,1], **Papiya Mitra Mazumder** [*,1]

[1] Department of Pharmaceutical Sciences & Technology, Birla Institute of Technology, Mesra, Ranchi, Jharkhand – 835215

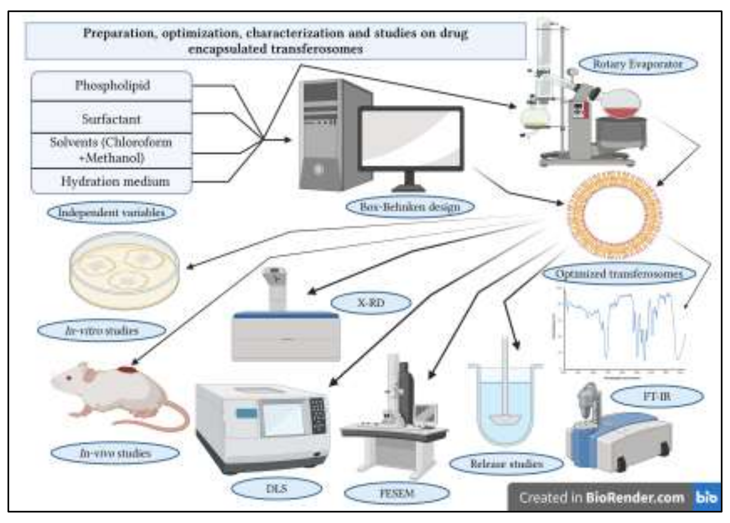
INTRODUCTION & AIM

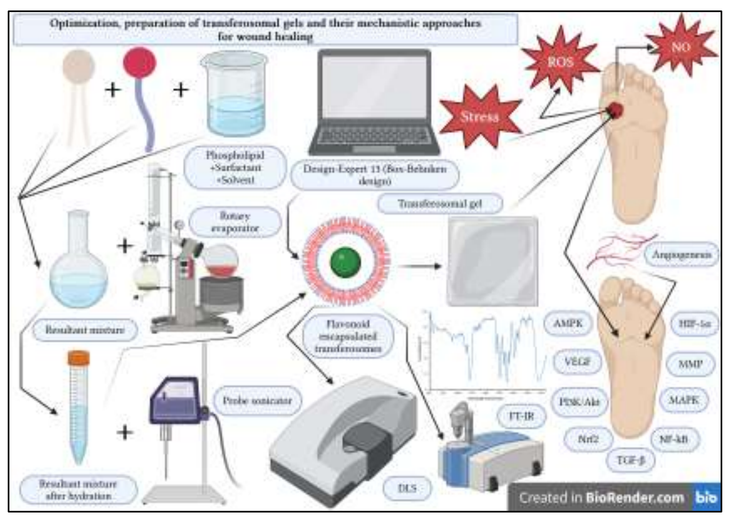
- Flavonoids are highly used natural phenolic compounds, which have shown potential role in wound healing.
- Flavonoids possess wound-healing properties based on anti-inflammatory, angiogenesis, re-epithelialization and antioxidant effects.
- Wound healing is an orchestrated mechanism involving phases like coagulation, inflammation, migration or proliferation and remodeling.



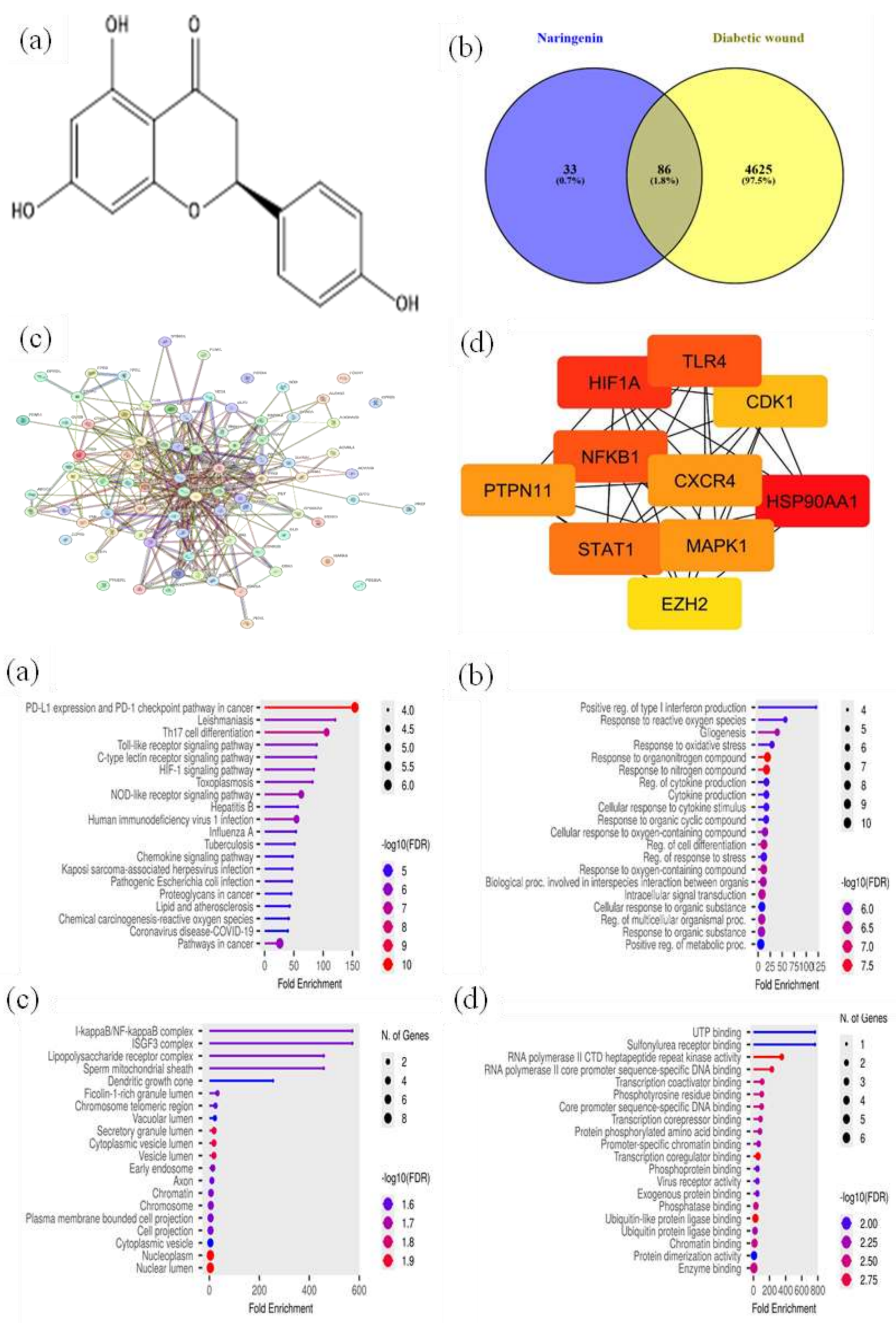


METHOD





Rotary film evaporation method or thin-film hydration technique.



Rank	Name	Score
1	HSP90AA1	39
2	HIF1A	36
3	NFKB1	26
3	TLR4	26
5	STAT1	21
6	PTPN11	19
6	MAPK1	19
6	CXCR4	19
9	CDK1	16
10	EZH2	15

Fig. 6: 2D structure of naringenin, Venn diagram, Full string network representation of common targets and Top 10 genes based on degree of interactions, GO and KEGG analysis.

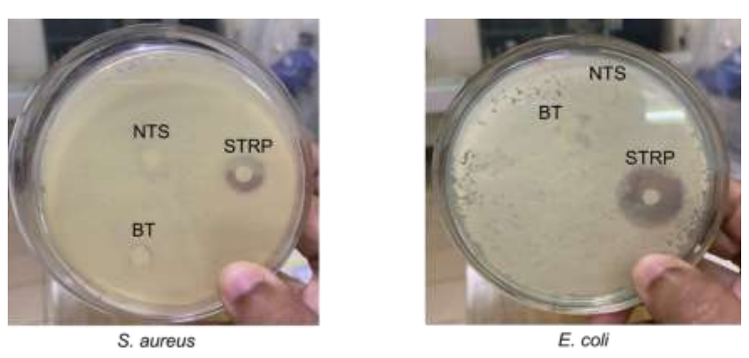


Fig. 7: Zone of inhibition (ZOI) of blank transferosomes (BT), naringenin encapsulated transferosomes (NTS) and streptomycin (STRP) against *S. aureus* and *E. coli*.

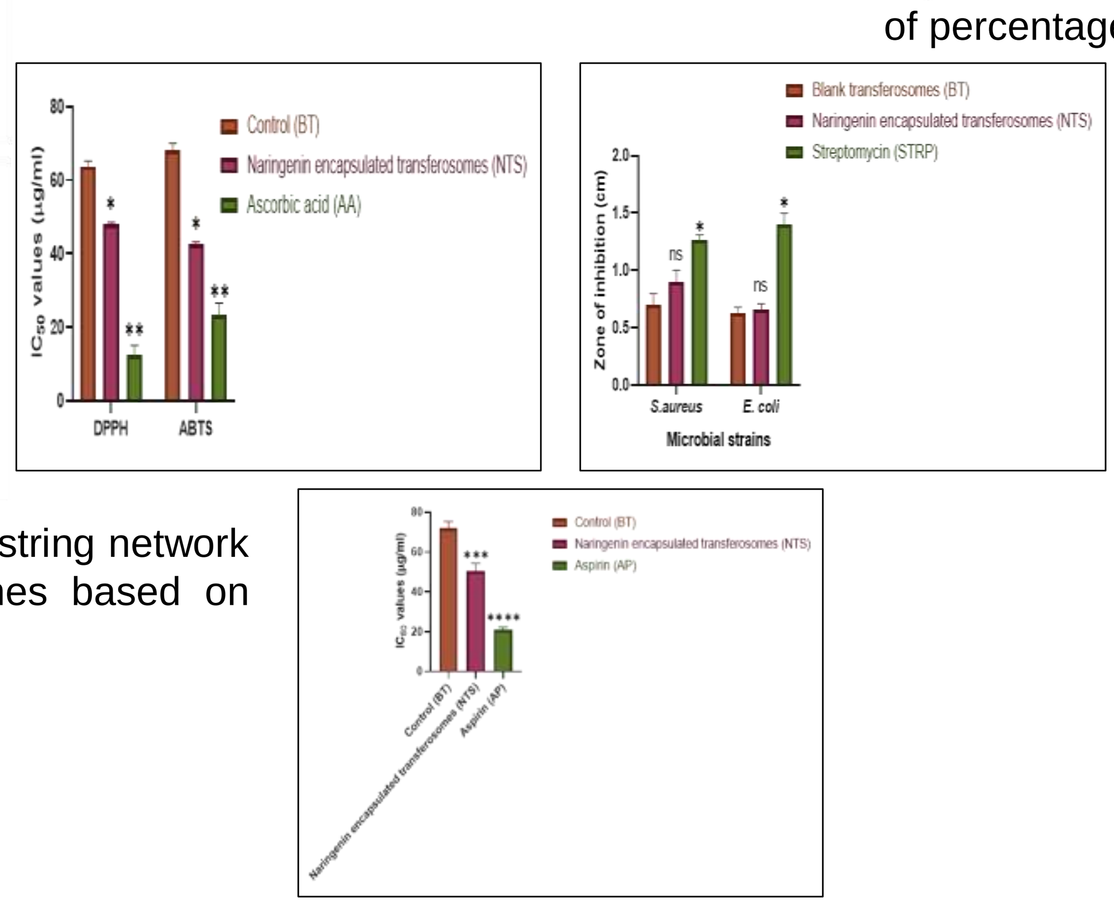


Fig. 8: *In vitro* antioxidant assay (DPPH and ABTS) of naringenin encapsulated transferosomes with ascorbic acid as standard, Antimicrobial assay (ZOI) of naringenin encapsulated transferosomes against (*S. aureus* and *E. coli*) with streptomycin as standard and *In vitro* anti-inflammatory assay of naringenin encapsulated transferosomes with aspirin as standard.

RESULTS & DISCUSSION

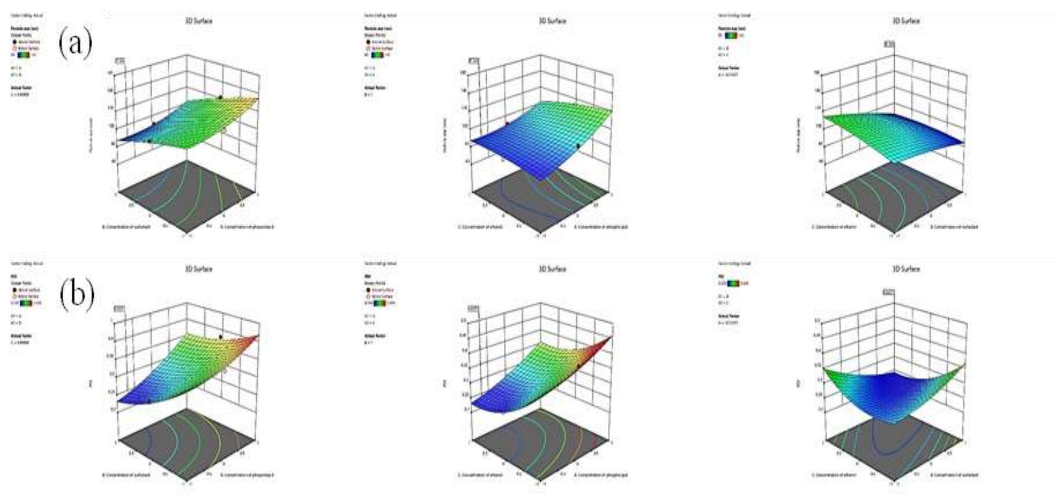


Fig. 1: 3D surface graph prepared using Design Expert Version 13.0.5.0

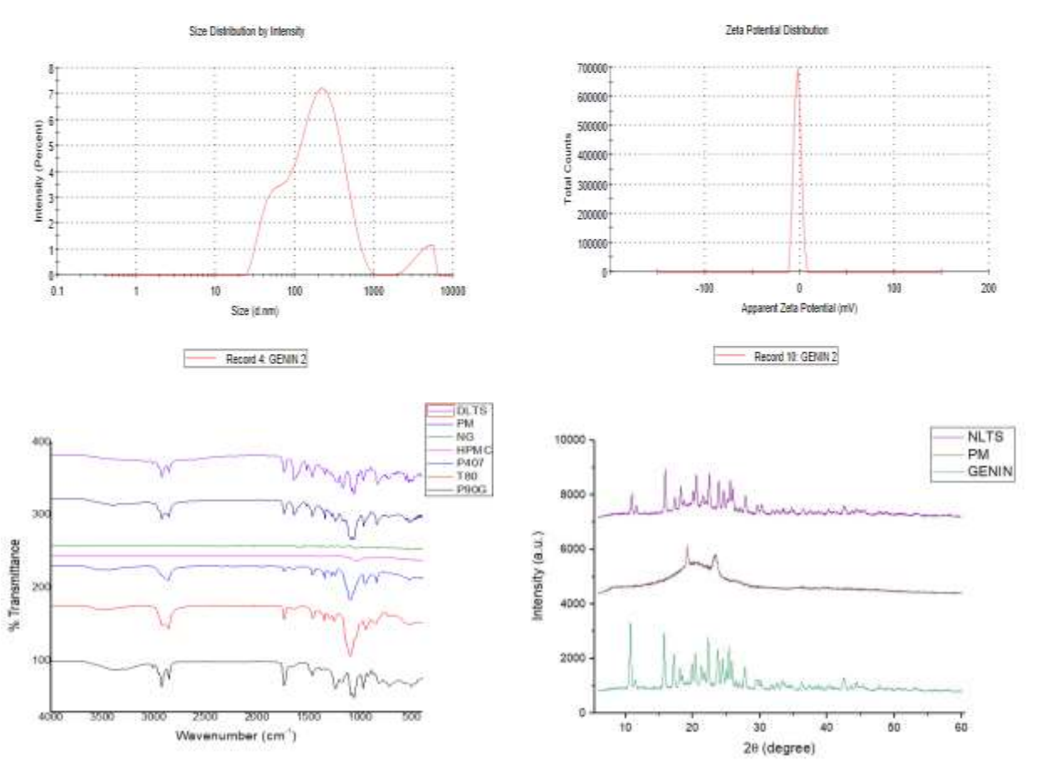


Fig. 2: Particle Size and Zeta Potential of naringenin encapsulated transferosomes, FT-IR studies of naringenin encapsulated transferosomes (DLTS), XRD of naringenin loaded transferosomes (NLTS).

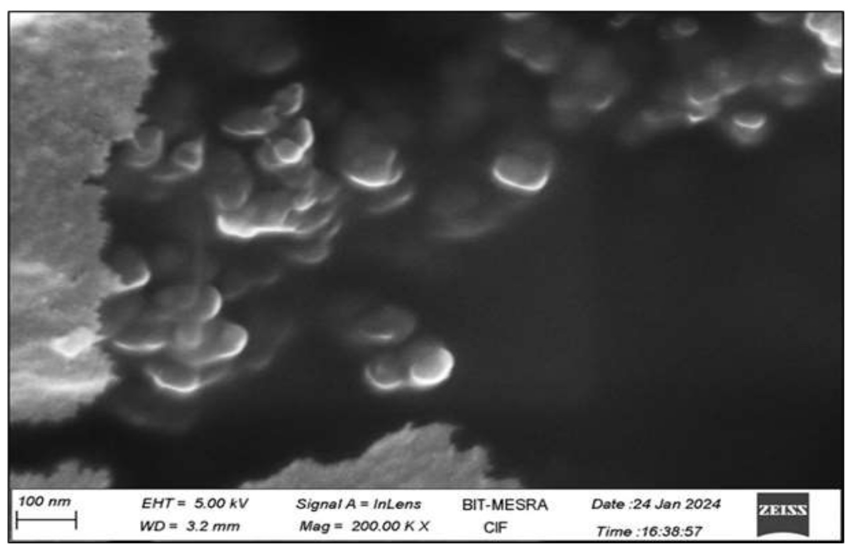


Fig. 3: FESEM images of naringenin embedded transferosomes at a magnification of 200 (K X).

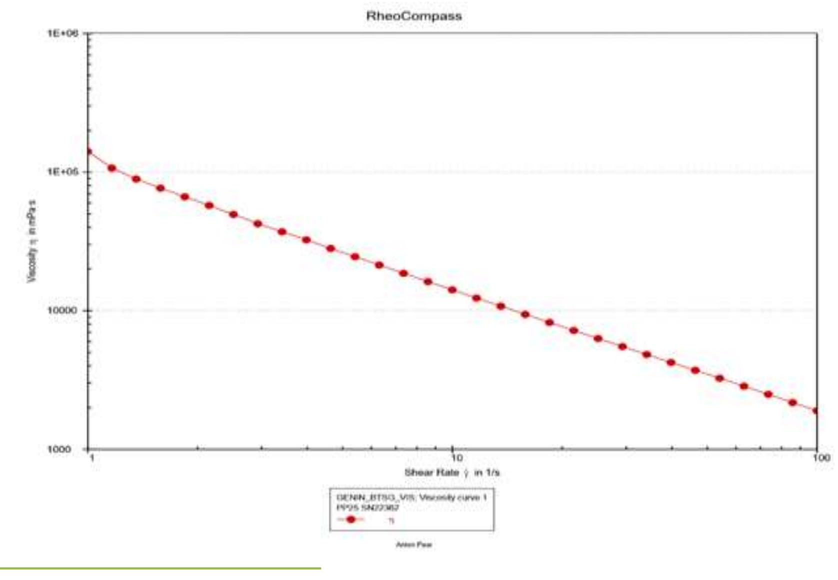


Fig. 5: Rheology studies of naringenin encapsulated transferosomal gel.

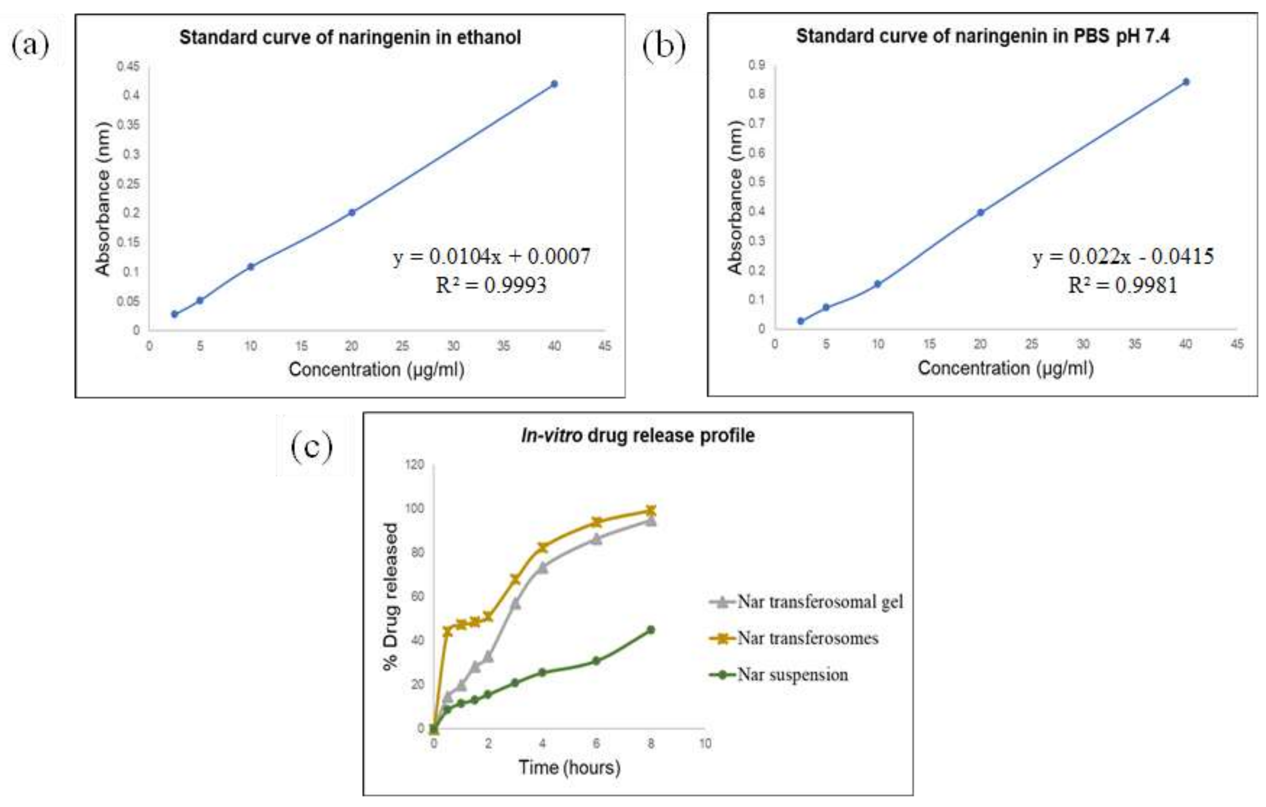
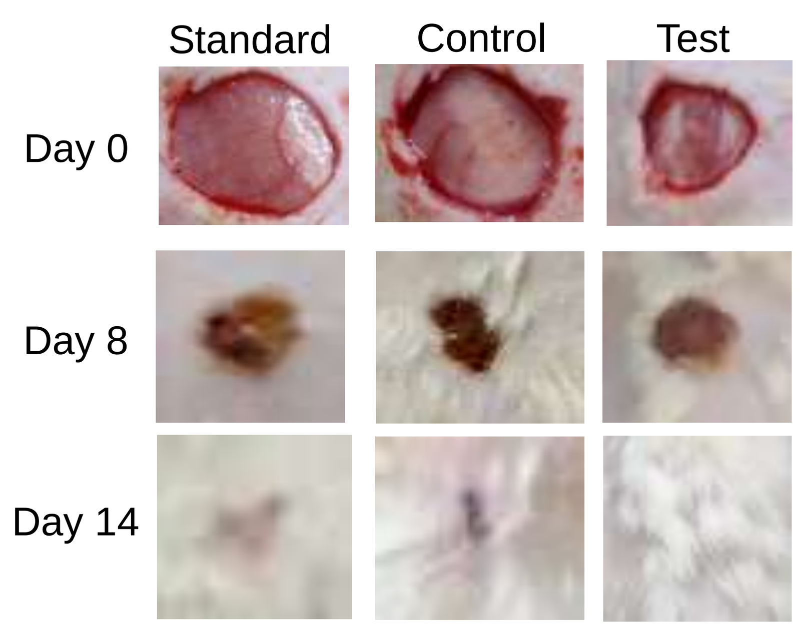


Fig. 4: Percentage entrapment efficiency and *In vitro* drug release profile of naringenin encapsulated transferosomal gel.



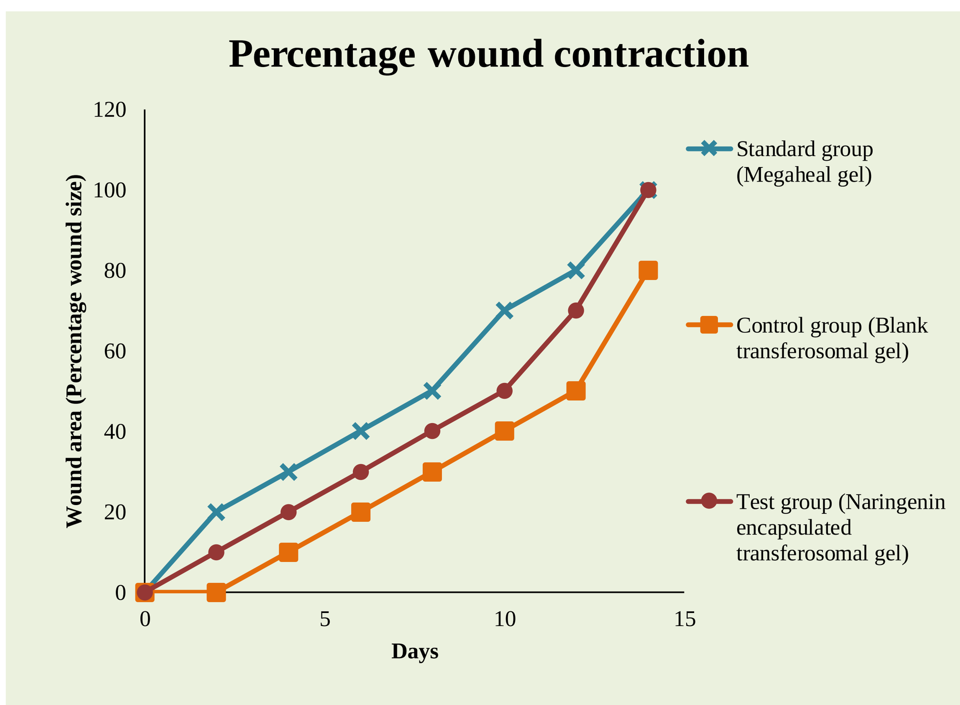


Fig. 9: *In vivo* studies based on wound healing process at different time intervals and calculation of percentage wound contraction.

CONCLUSION

Flavonoids have an excellent pharmacological profile but being BCS Class II or Class IV drugs they go through multiple issues. Although with suitable novel drug delivery system (transferosomes), flavonoids can be delivered to the selected site along with proper onset and duration of action which results in better bioavailability. Here, focus has been made on naringenin and its further encapsulation utilizing transferosomal gel which have shown enough potential to treat diabetic wounds. Network pharmacology, *in vitro and in vivo* studies provide an assurance about the wound healing potential of naringenin encapsulated transferosome infused gel.

REFERENCES

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- Chowdhury A, Mitra Mazumder P. Unlocking the potential of flavonoid-infused drug delivery systems for diabetic wound healing with a mechanistic exploration. Inflammopharmacology. 2024;32(5):2861-2896.