

OrD FG session

Marwa A. Sallam

CRS 2022 Annual Meeting & Expo

July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada

Advanced Delivery Science

Nanomedicine Implementations of dietary supplements in breast cancer therapy

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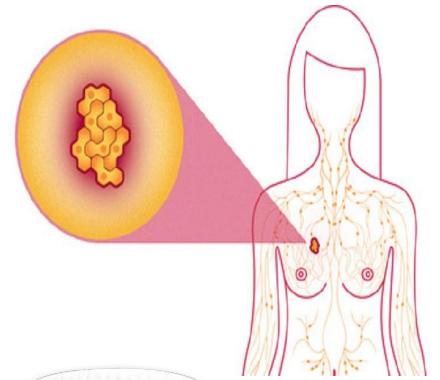
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Breast cancer

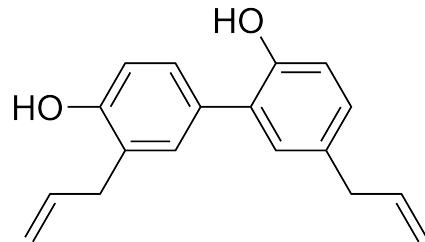
- Breast cancer (BC) is considered as the second common type of cancer after lung cancer and is currently showing the highest incidence rate in females among different cancer types .
- Many reports suggested that by 2050, breast cancer will spread to reach about 3.2 million new cases.
- As a public health concern , new strategies should be implemented to overcome the main restrictions of chemotherapy as random biodistribution, systemic toxicity & multidrug resistance.



Dietary products for BC

- Polyphenolic compound
herbal extract of *Magnolia grandiflora* seeds
-Induce apoptosis of cancer cells
- HK suppresses P-glycoprotein efflux pumps to increase sensitivity of drug-resistant tumor cells chemotherapeutic drugs

Honokiol



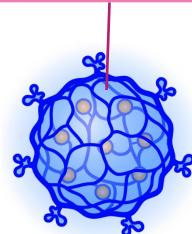
Pemetrexed

Multi-directional antifolate cytotoxic chemotherapeutic drug against different types of cancer including breast cancer

limited clinical benefits
poor therapeutic results due to inability to achieve sufficient intracellular concentrations at the dose limits allowed, while increasing the PMT dose results in systemic toxicit & MDR

So, combining HK with PMT can help overcoming the MDR and improve the antitumor efficacy

biodegradability, biocompatibility



Self assembled protein polysaccharide nanogels

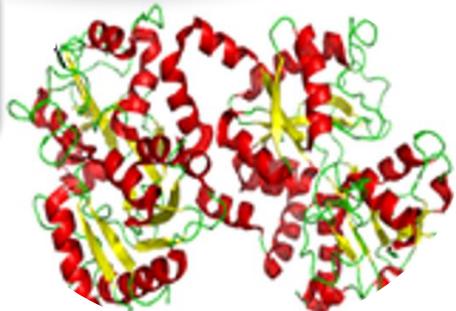
- negligible toxicity profiles

ease of functionalization

Self-assembled Lactoferrin Carboxymethyl Cellulose Nanogels for Synergistic Chemo/herbal Breast Cancer Therapy

Lactoferrin

Immunomodulatory
anti-inflammatory,
anticancer

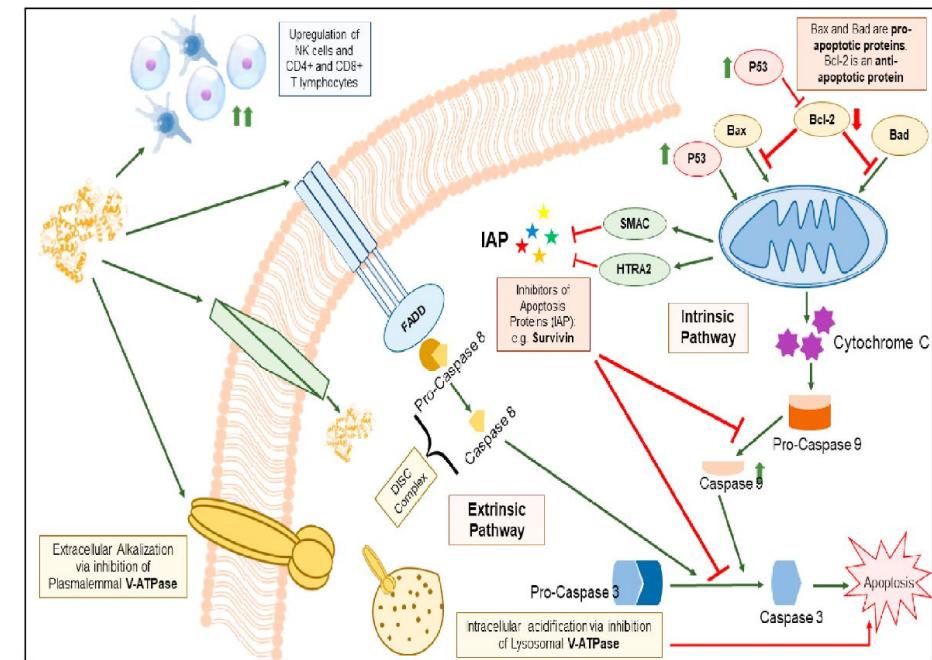


functional groups allow
its chemical conjugation

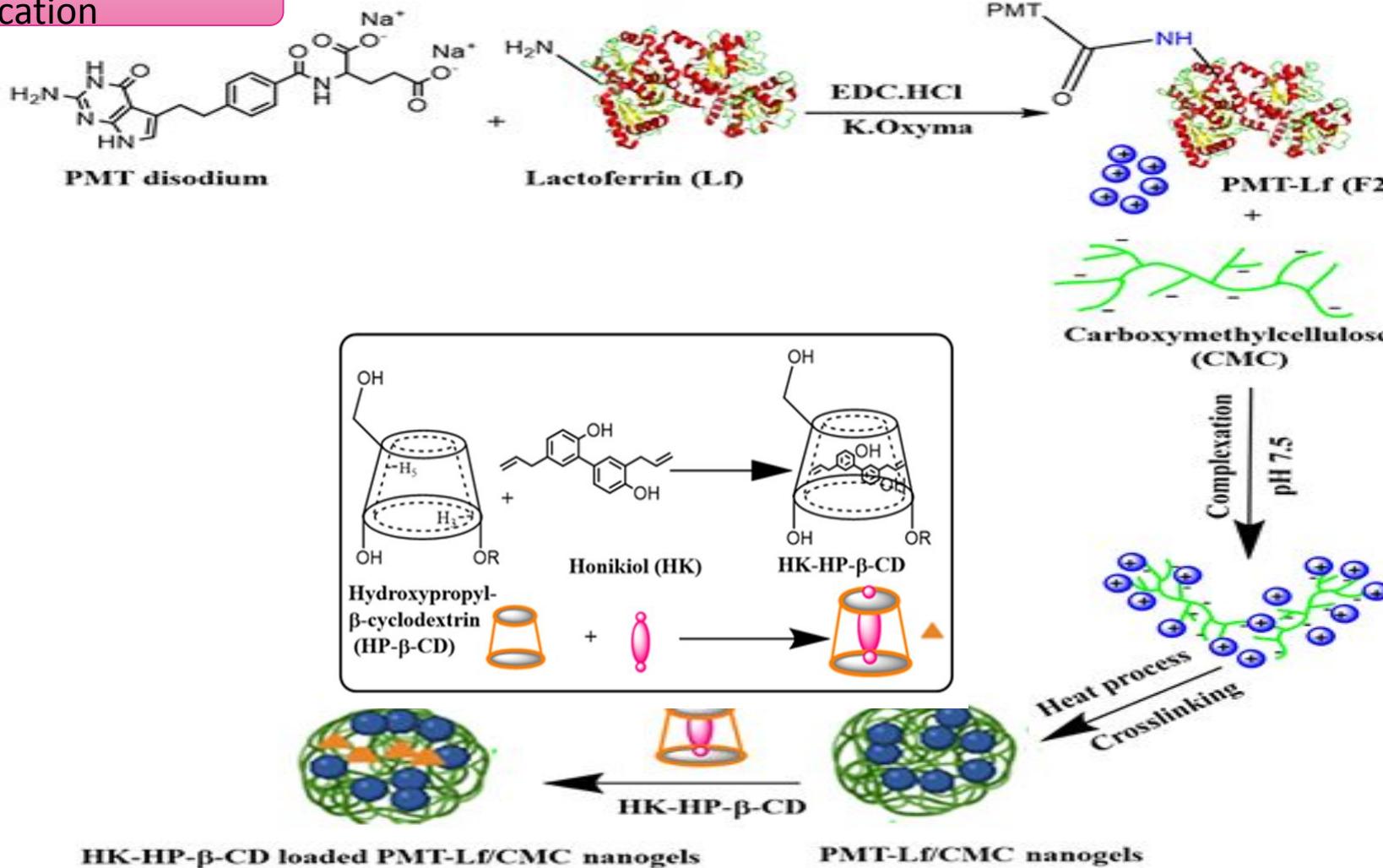
Secreted by mucosal epithelial cells
A component of most biological
fluids

Milk

Targeting ligand
affinity to bind to receptors
overexpressed on tumor cells
including LF-receptors (LRP1,
LRP2) and low-density lipoprotein
(LDL).



Dual drug loaded Nanogel fabrication

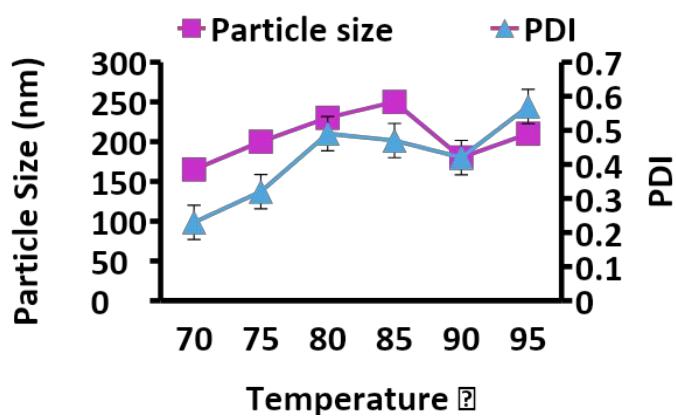
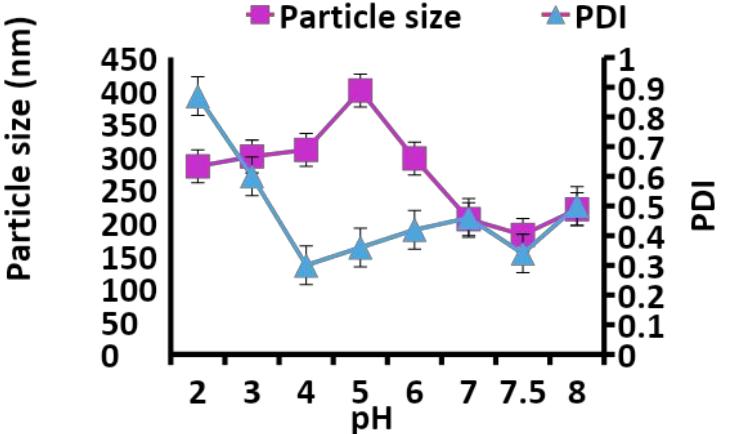
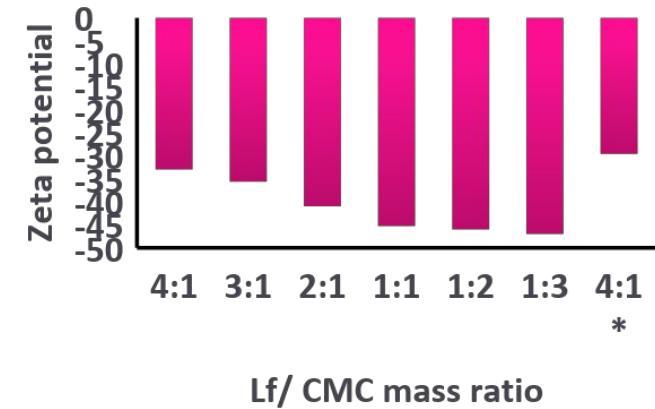
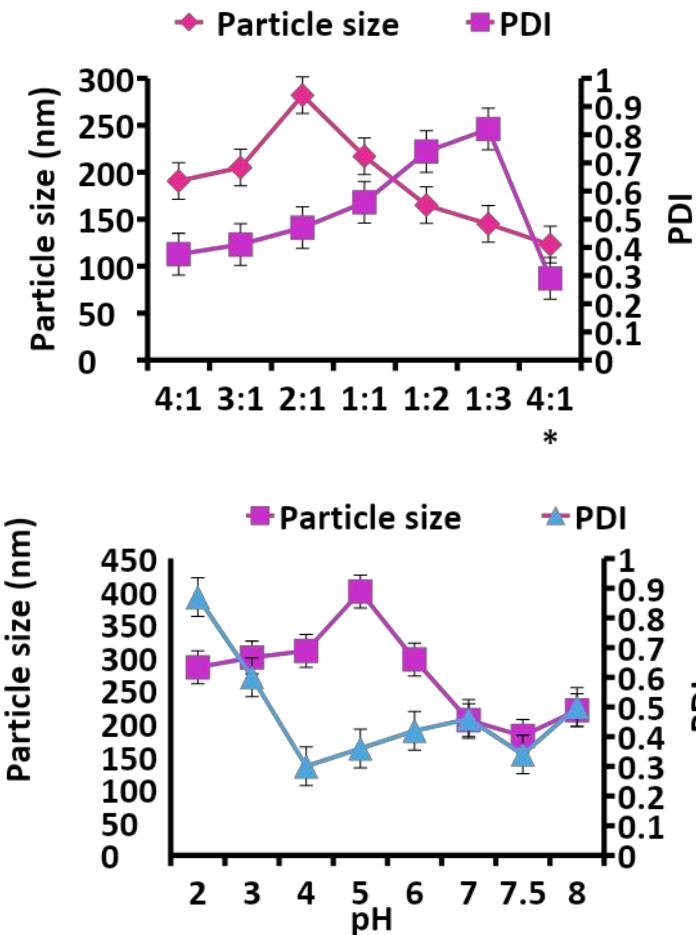
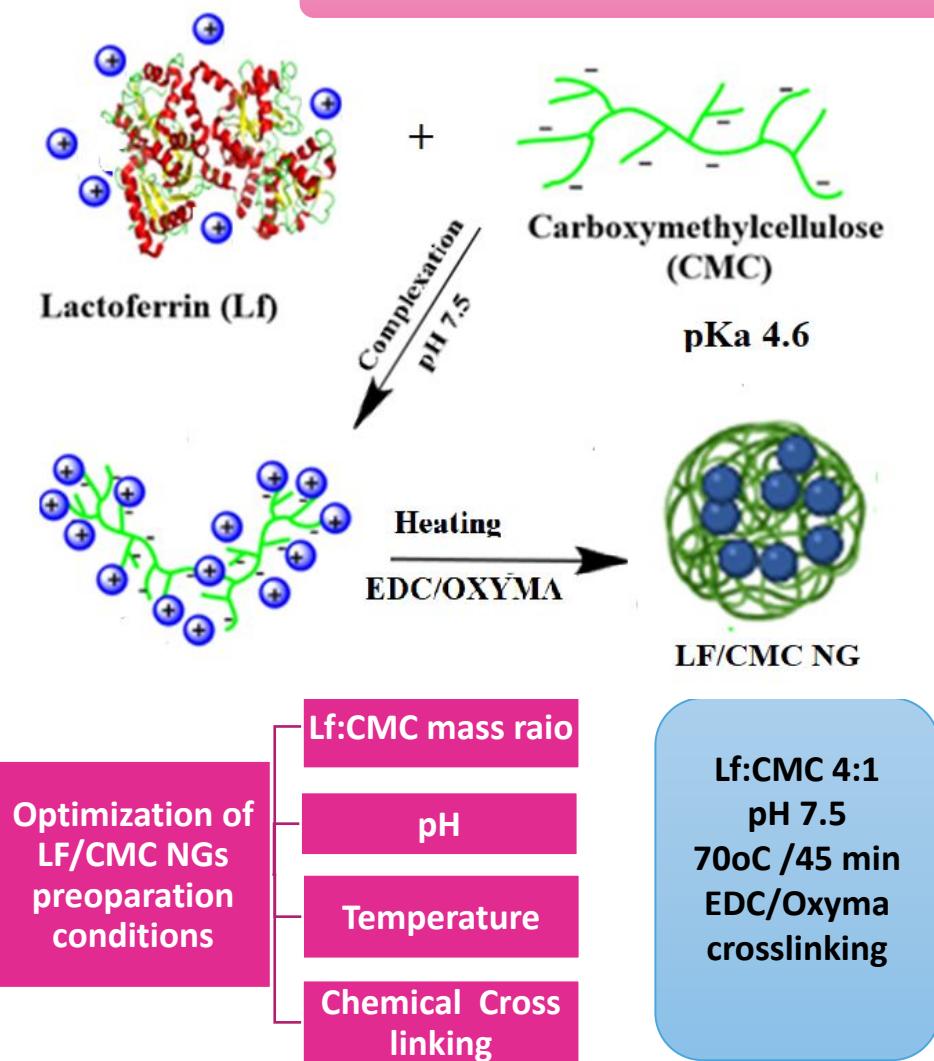


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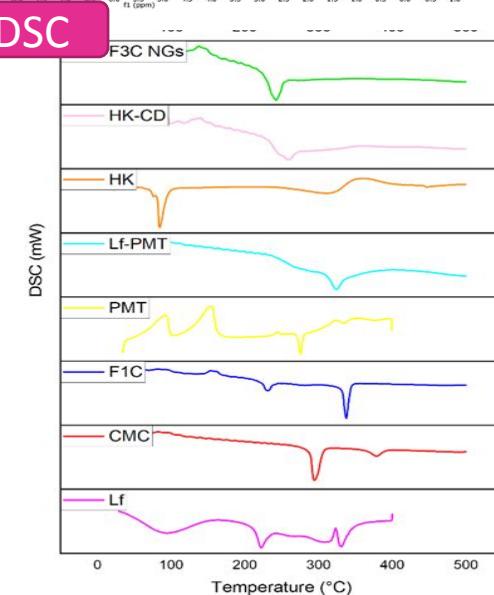
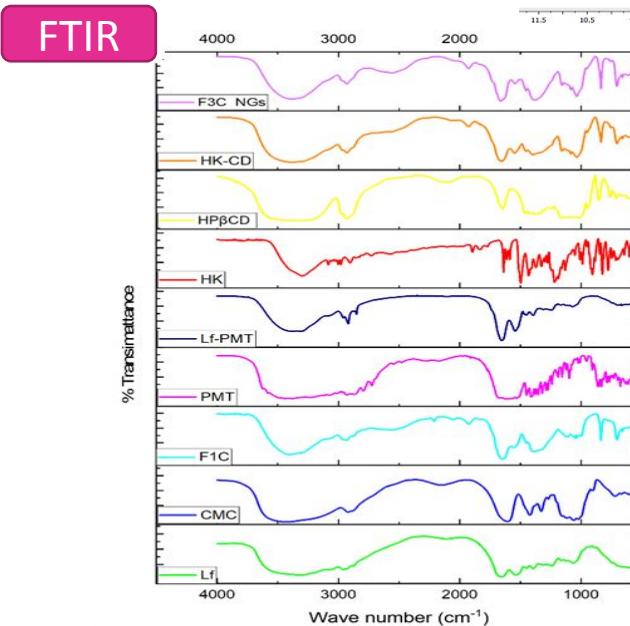
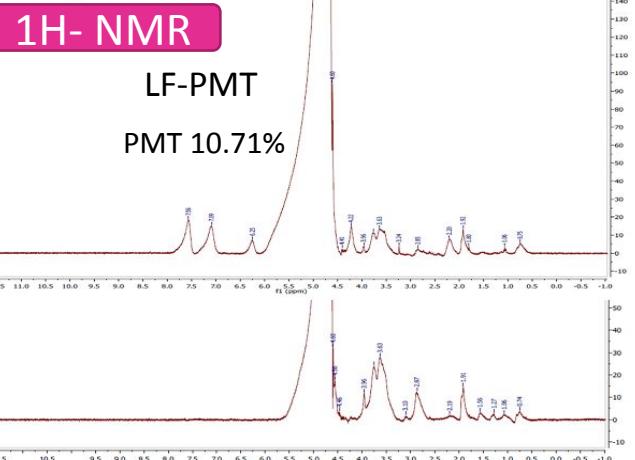
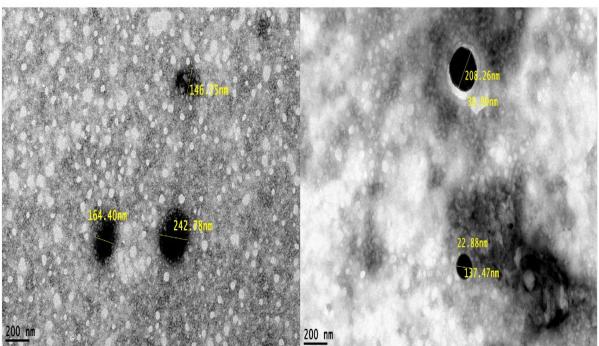
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Fabrication of LF/CMC Nanogels



Physico-chemical characterization

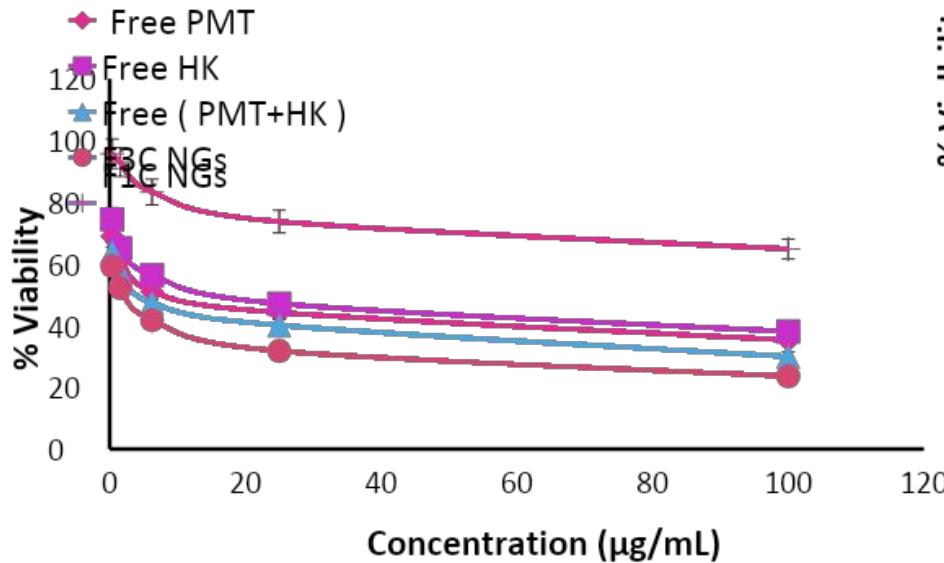
Formulation	Particle Size (nm)	Zeta Potential (mV)	PDI
F1(LF/CMC, uncross linked NG)	165.0\pm0.71	-32.0 \pm0.8	0.230\pm0.003
F1C (LF/CMC, cross linked NG)	123.0 \pm0.09	-28.9 \pm0.7	0.290\pm0.002
F2 (LF-PMT)	206.3\pm0.32	+14.7 \pm0.5	0.389\pm0.021



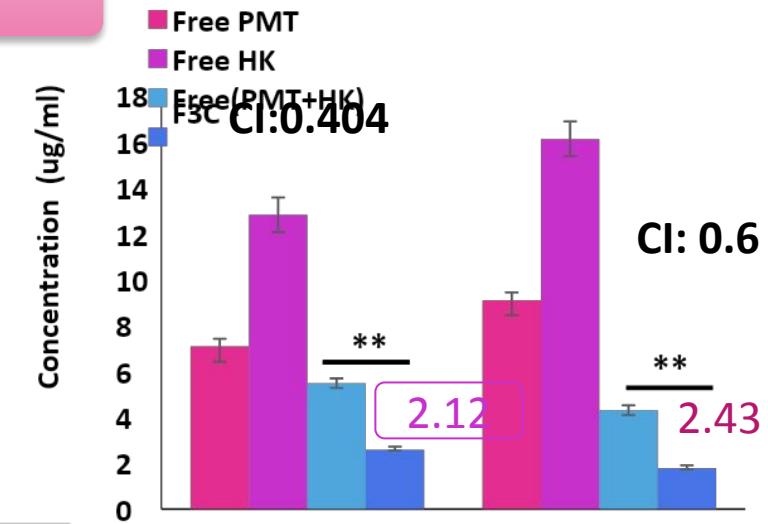
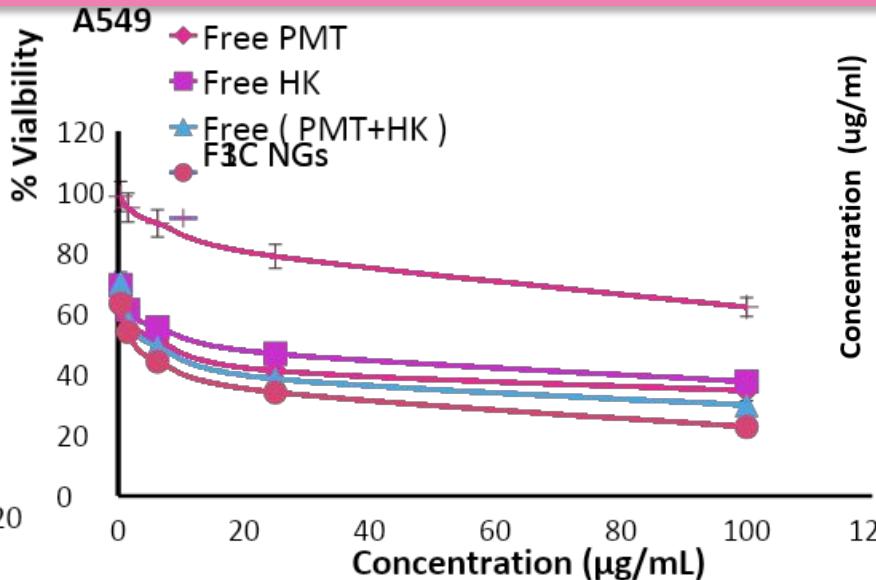
Formula	Particle Size (nm)	Zeta Potential (mV)	PDI	% HK content	%PMT content
F3U (HK/PMT, uncross linked NG)	273.1\pm 0.45	- 41.2 \pm0.8	0.300\pm0.012	4.50\pm 0.08	2.164 \pm0.07
F3C (HK/PMT, cross linked NG)	193.4\pm0.2	-34.5 \pm0.7	0.230\pm0.001	4.55\pm 0.07	2.171 \pm0.17



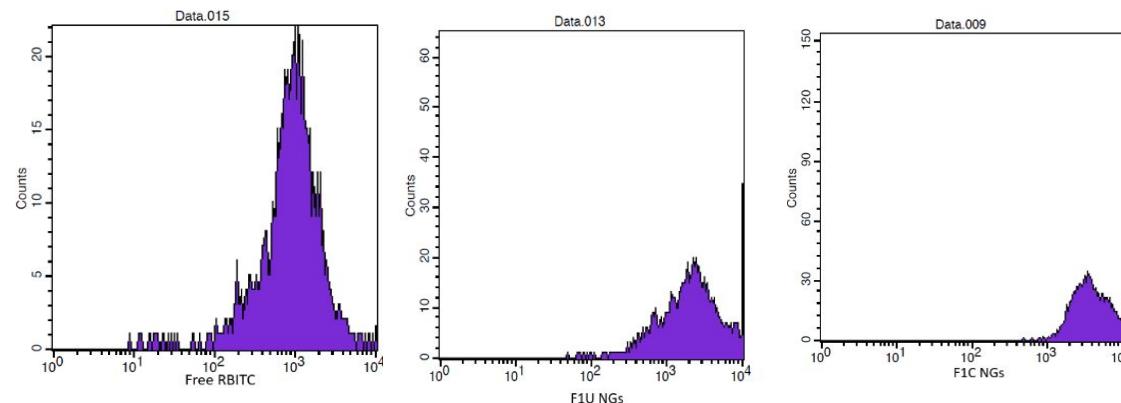
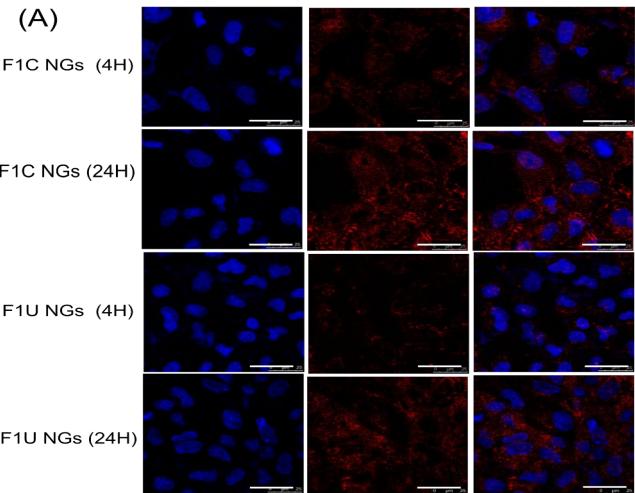
MDA-MB-231



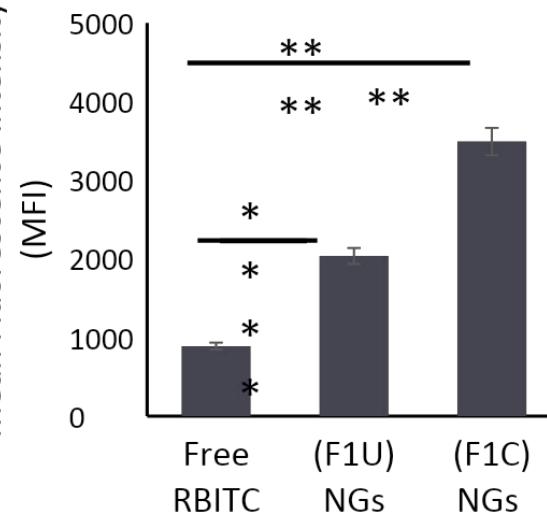
Invitro cell studies



(A)



Mean Fluorescence Intensity (MFI)



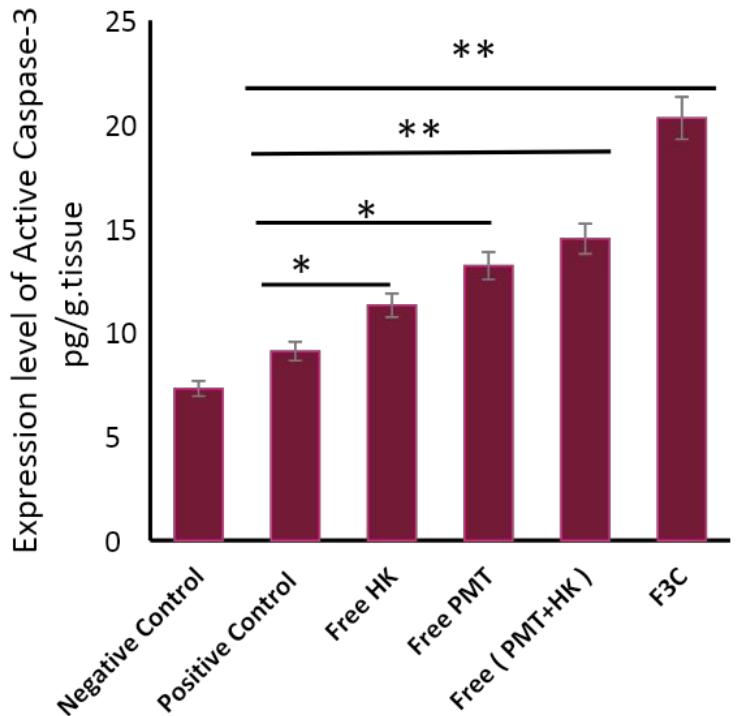
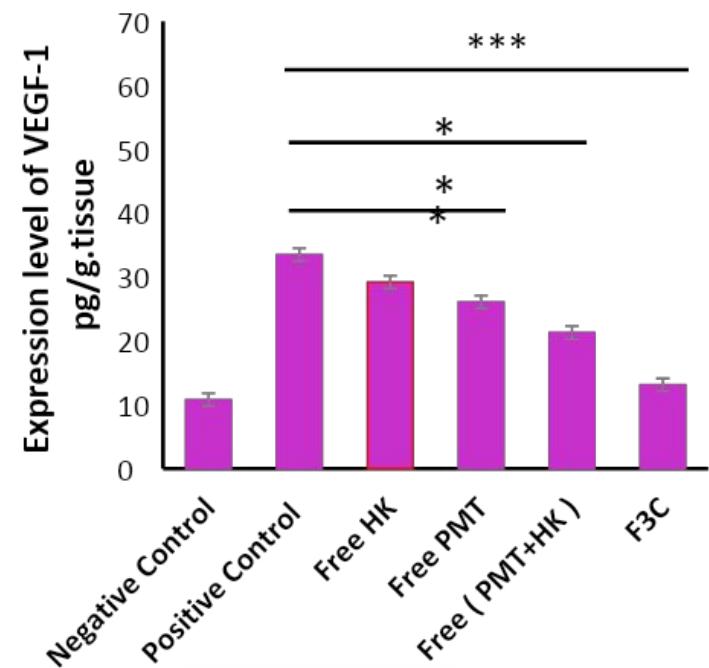
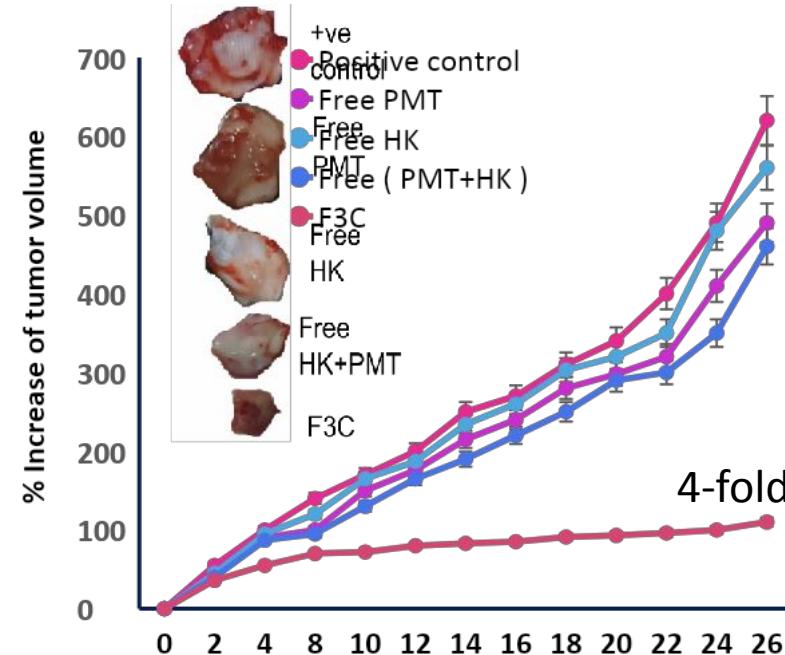
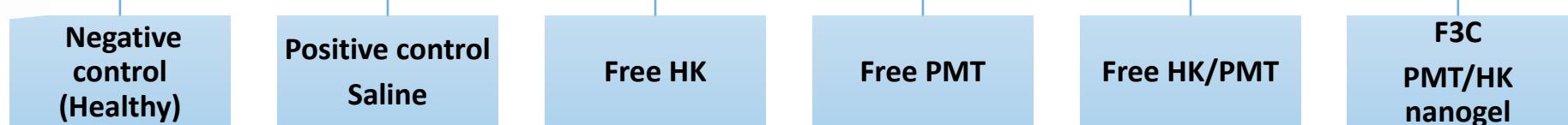
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In vivo antitumor efficacy

EAC model



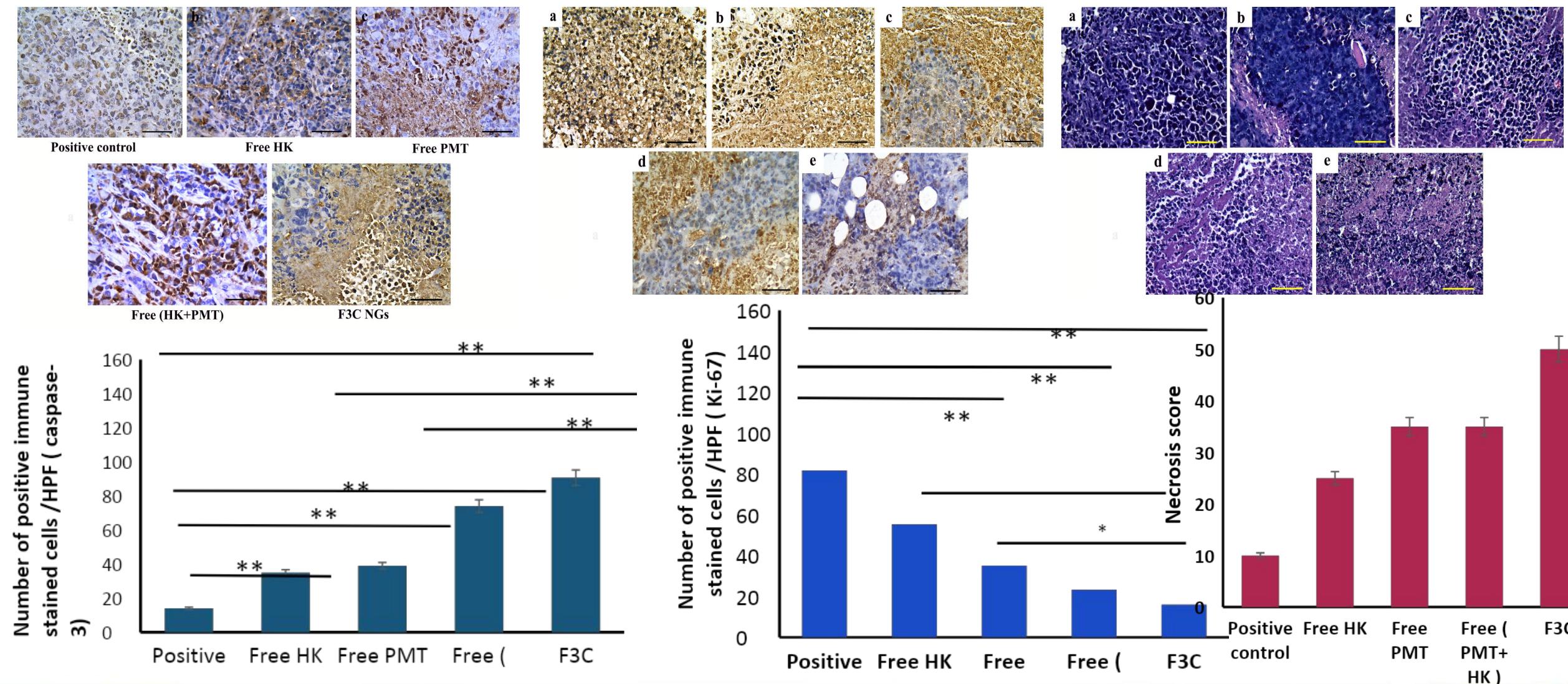
Time (Days)
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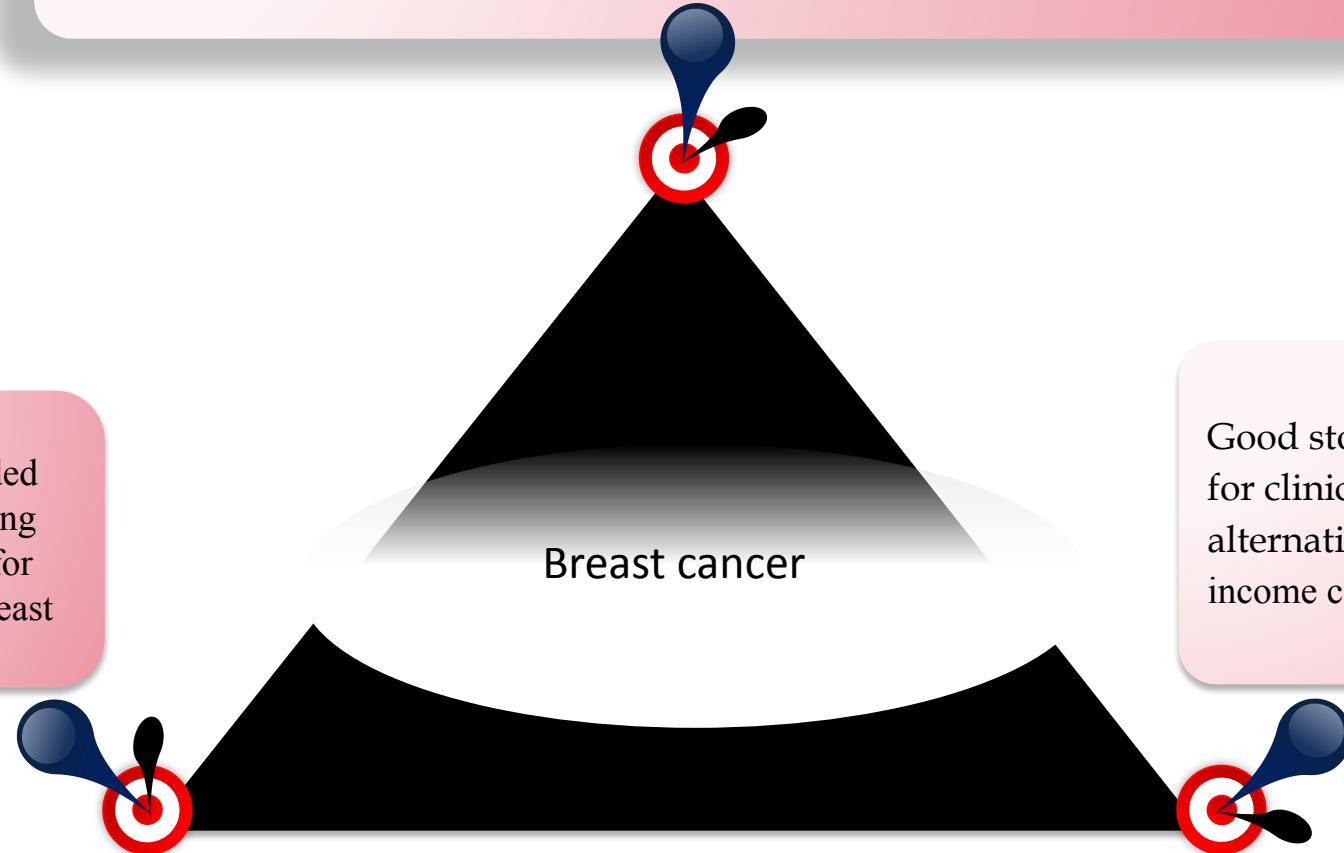
Immunohistochemical analysis



Conclusion

we fabricated of self-assembled nanogels utilizing hydrophilic biocompatible protein, lactoferrin (Lf) and polysaccharide carboxy methyl cellulose (CMC), for combined delivery of antimetabolite pemetrexed (PMT) and a herbal polyphenol honokiol (HK).

The green fabricated self-assembled dual loaded nanogel offers a promising biocompatible strategy for targeted combinatorial breast cancer therapy.



Good storage stability suggesting possibility for clinical translation providing an alternative for patient treatment in middle-low income countries



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