

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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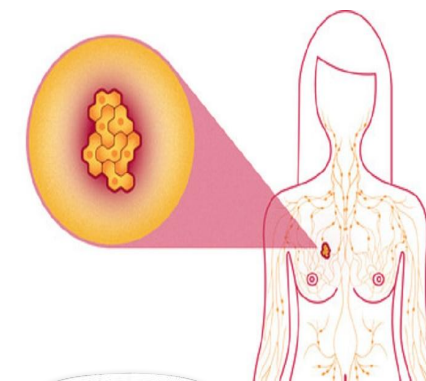
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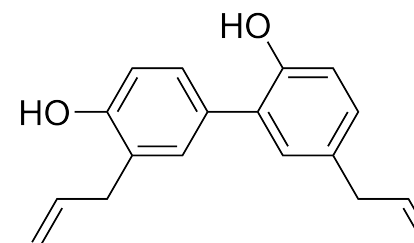
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Breast cancer

- 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.



Honokiol



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



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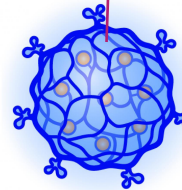
Pemetrexed

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 toxicity & 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



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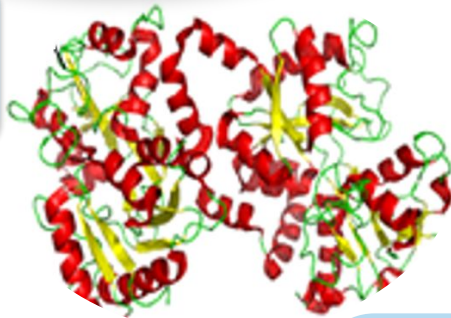
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Self-assembled Lactoferrin Carboxymethyl Cellulose Nanogels for Synergistic Chemo/herbal Breast Cancer Therapy

Lactoferrin

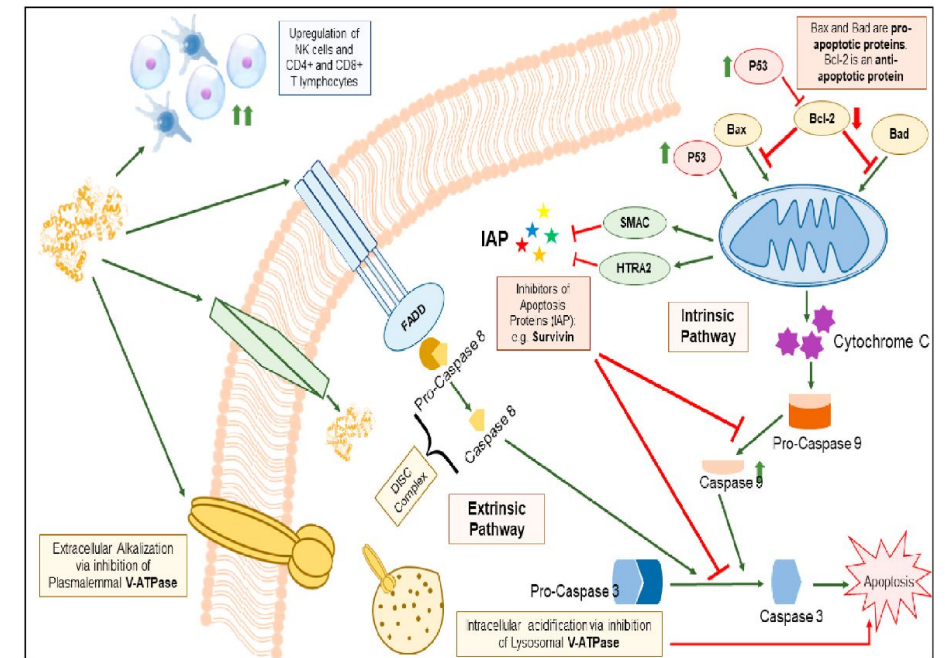
Immunomodulatory
anti-inflammatory,
anticancer



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).

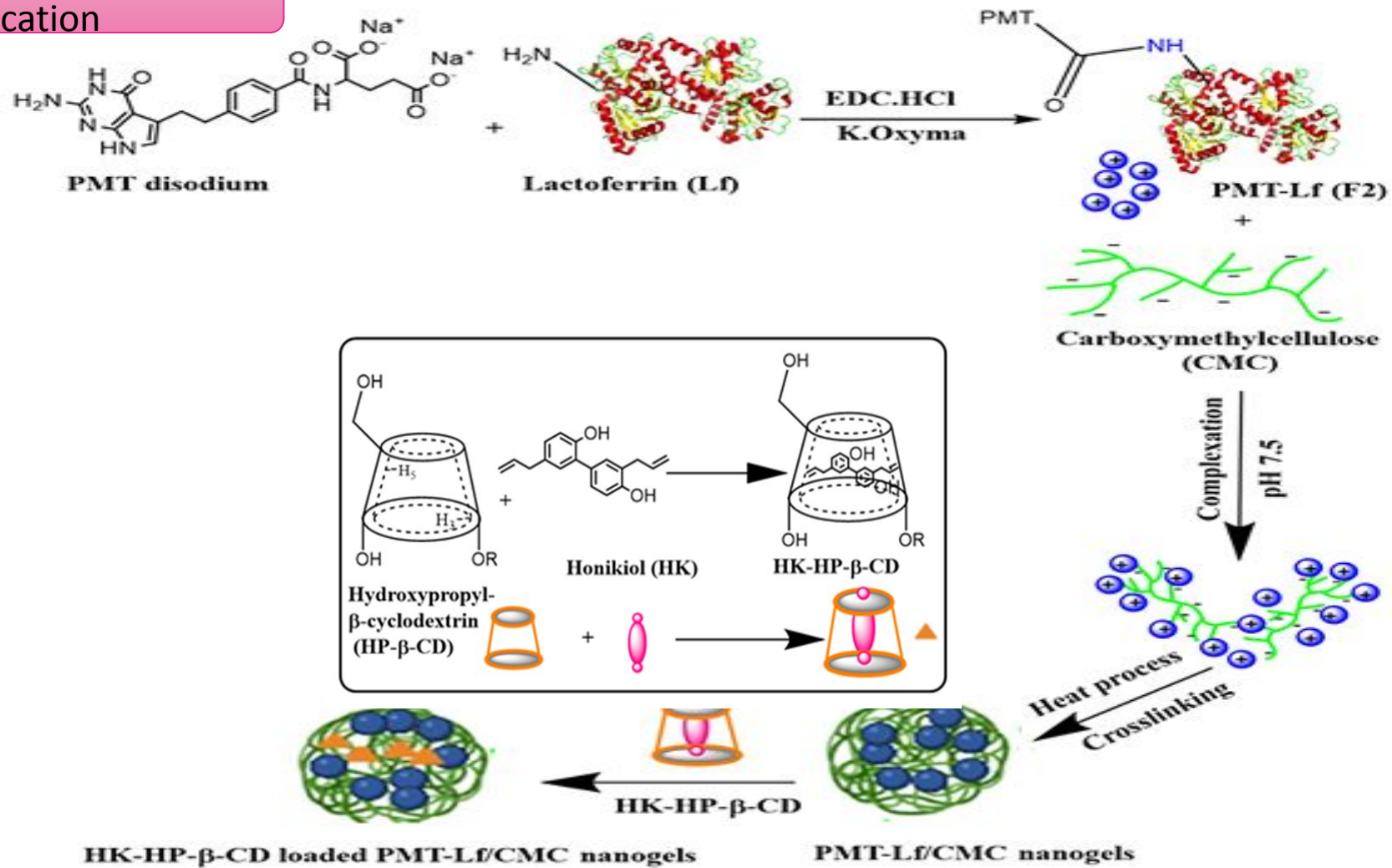


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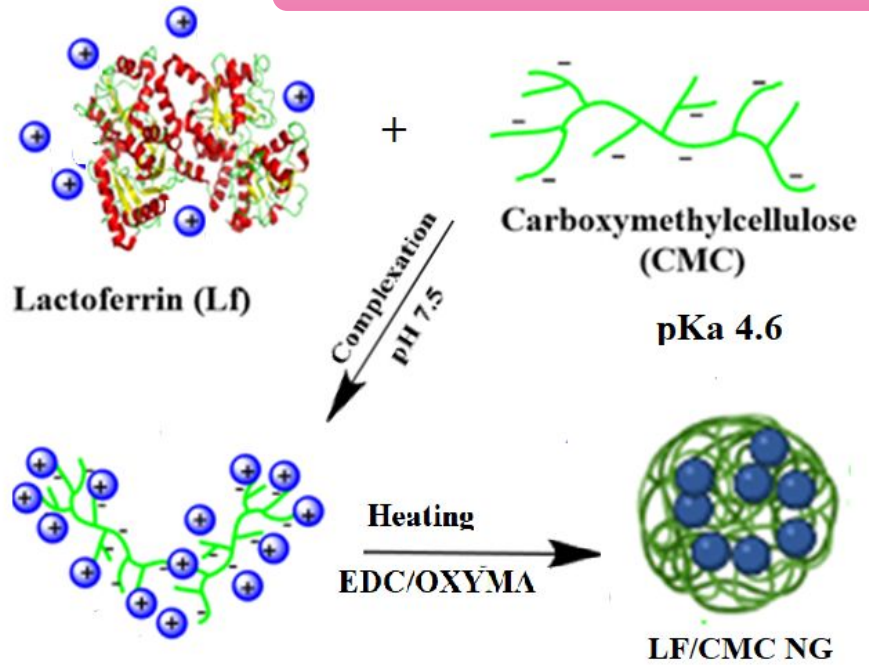
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Dual drug loaded Nanogel fabrication



Fabrication of LF/CMC Nanogels



Optimization of LF/CMC NGs preparation conditions

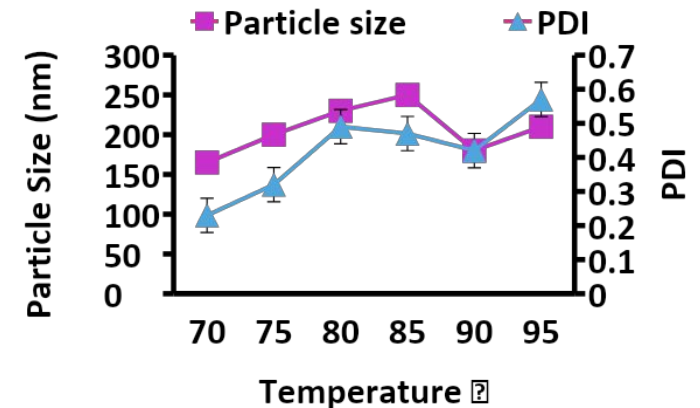
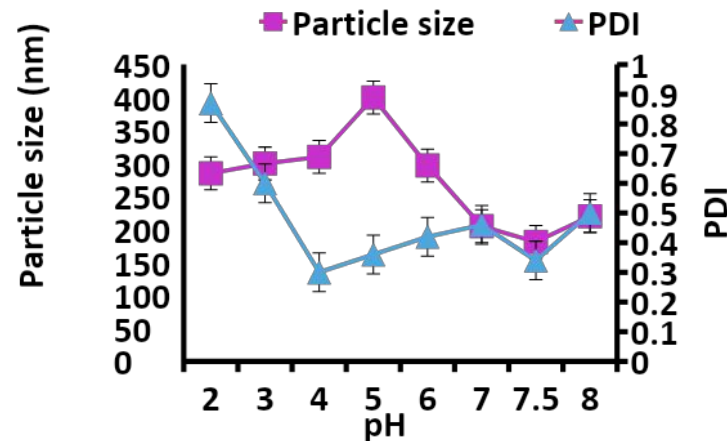
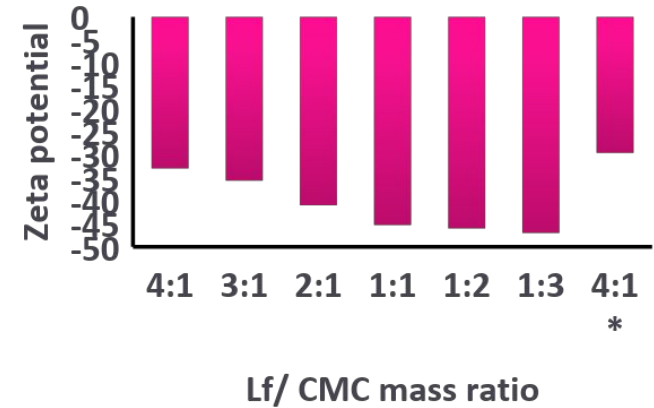
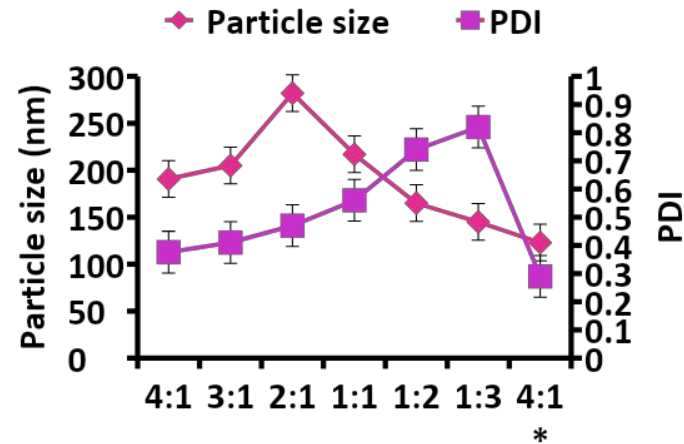
Lf:CMC mass ratio

pH

Temperature

Chemical Cross linking

Lf:CMC 4:1
pH 7.5
70°C / 45 min
EDC/OxyMA crosslinking



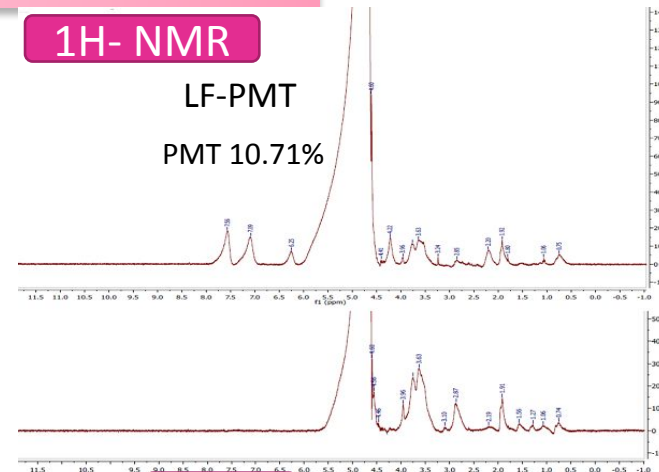
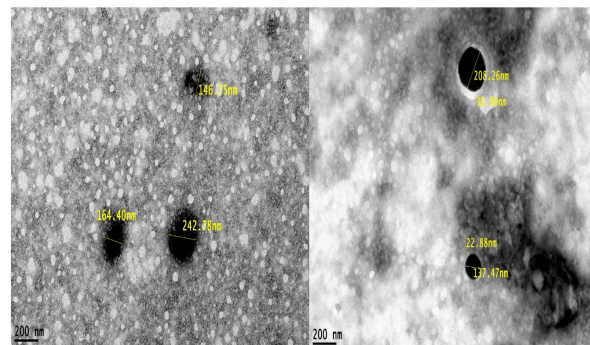
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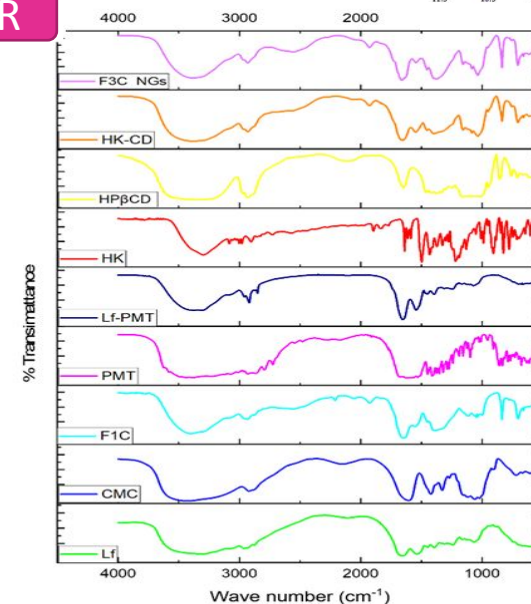
Physico-chemical characterization

Formulation	Particle Size (nm)	Zeta Potential (mV)	PDI
F1(LF/CMC, uncross linked NG)	165.0±0.71	-32.0 ±0.8	0.230±0.003
F1C (LF/CMC, cross linked NG)	123.0 ±0.09	-28.9 ±0.7	0.290±0.002
F2 (LF-PMT)	206.3±0.32	+14.7 ±0.5	0.389±0.021

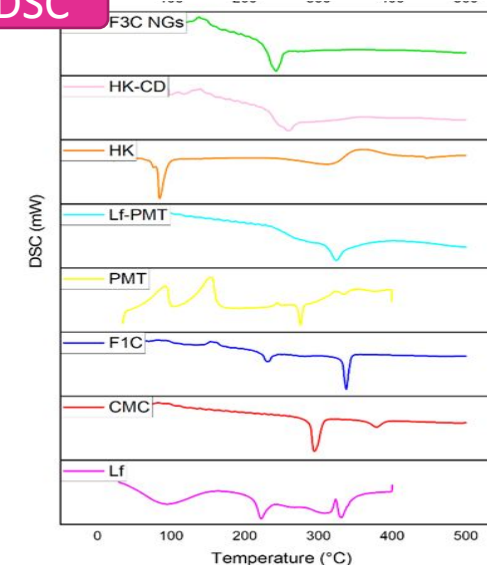


Formula	Particle Size (nm)	Zeta Potential (mV)	PDI	% HK content	%PMT content
F3U (HK/PMT, uncross linked NG)	273.1±0.45	- 41.2 ±0.8	0.300±0.012	4.50± 0.08	2.164 ±0.07
F3C (HK/PMT, cross linked NG)	193.4±0.2	-34.5 ±0.7	0.230±0.001	4.55± 0.07	2.171 ±0.17

FTIR



DSC



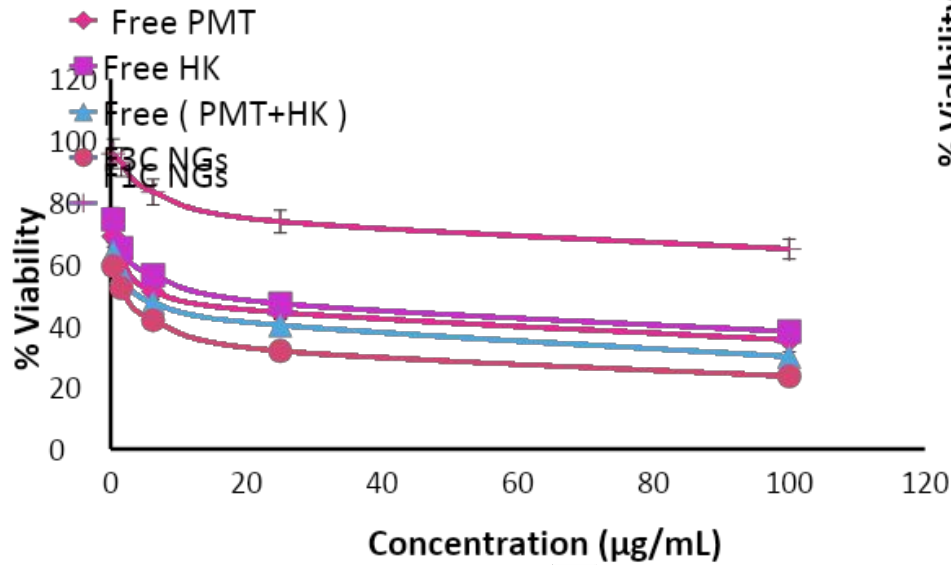
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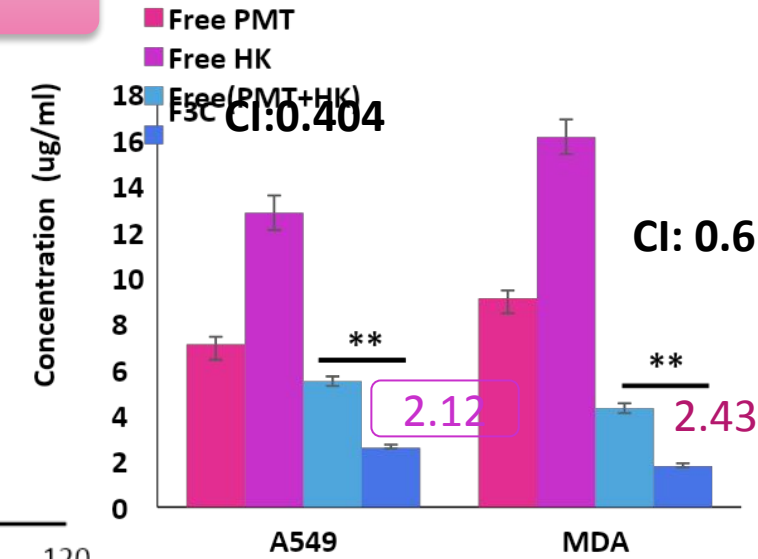
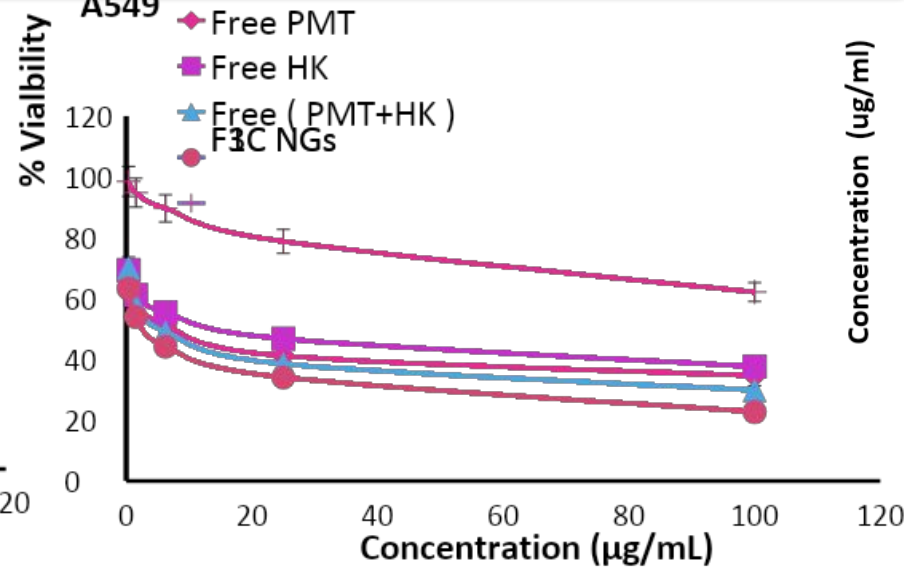
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Invitro cell studies

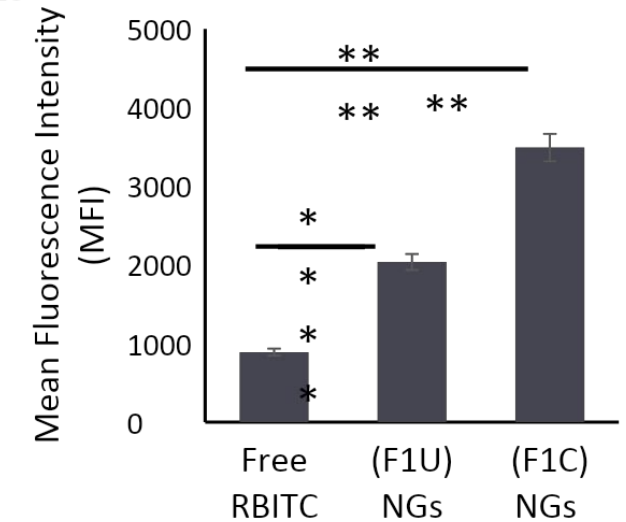
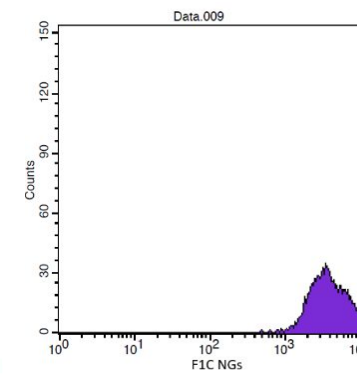
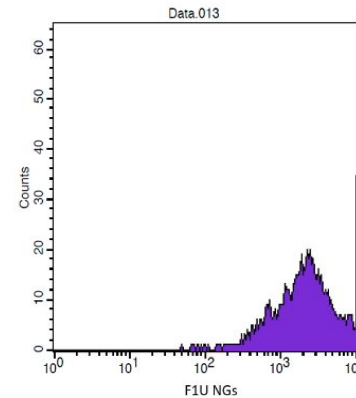
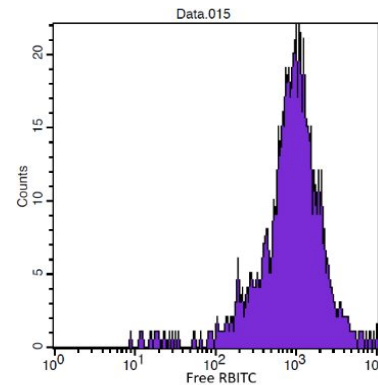
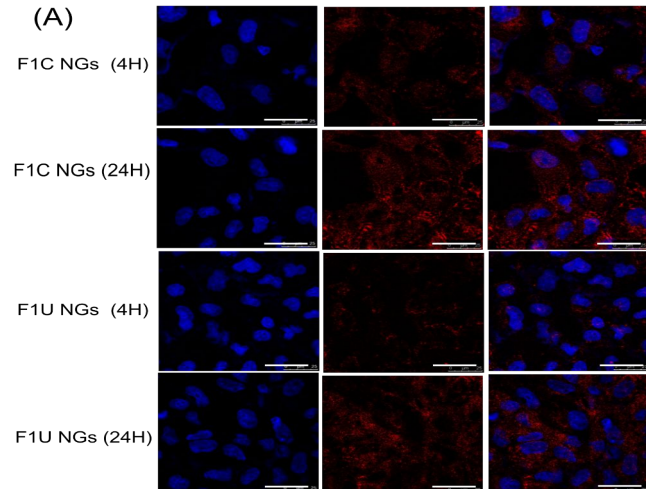
MDA-MB-231



A549



(A)



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In vivo antitumor efficacy

EAC model



3 treatments /week
3 weeks

Negative control
(Healthy)

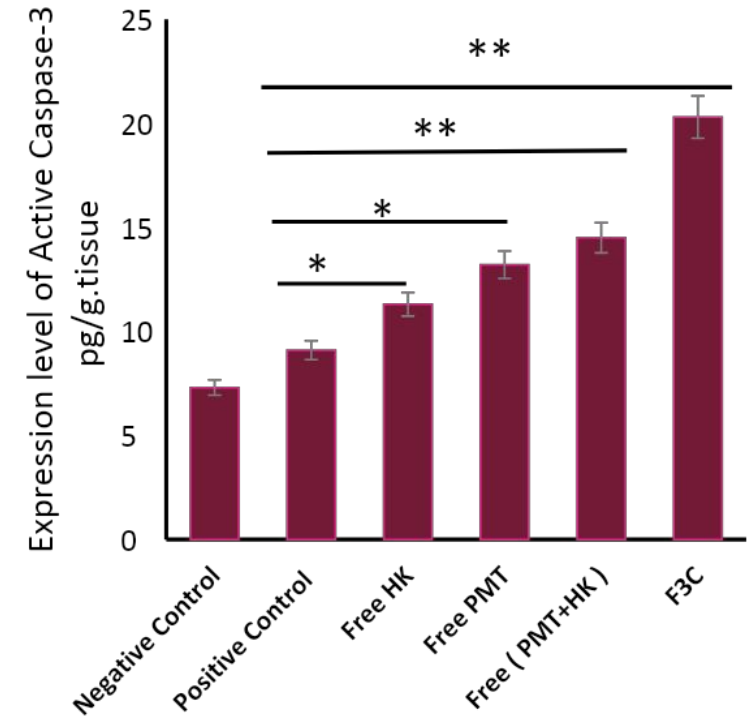
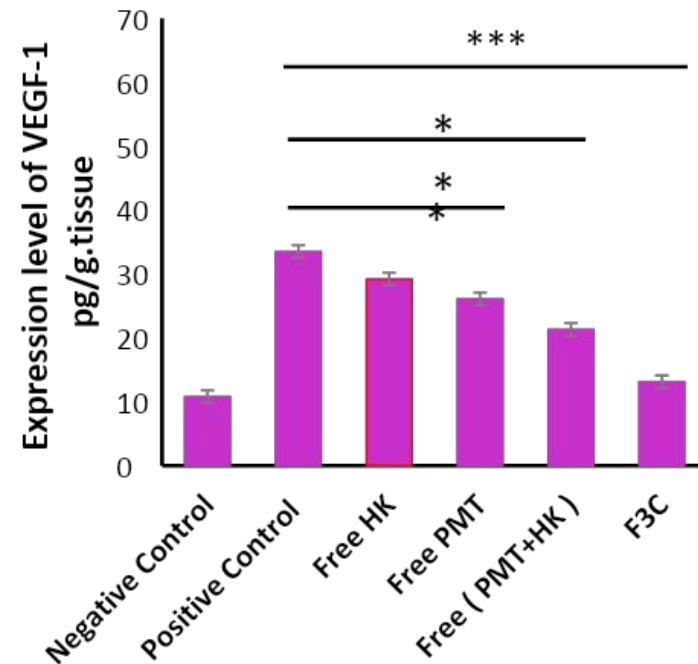
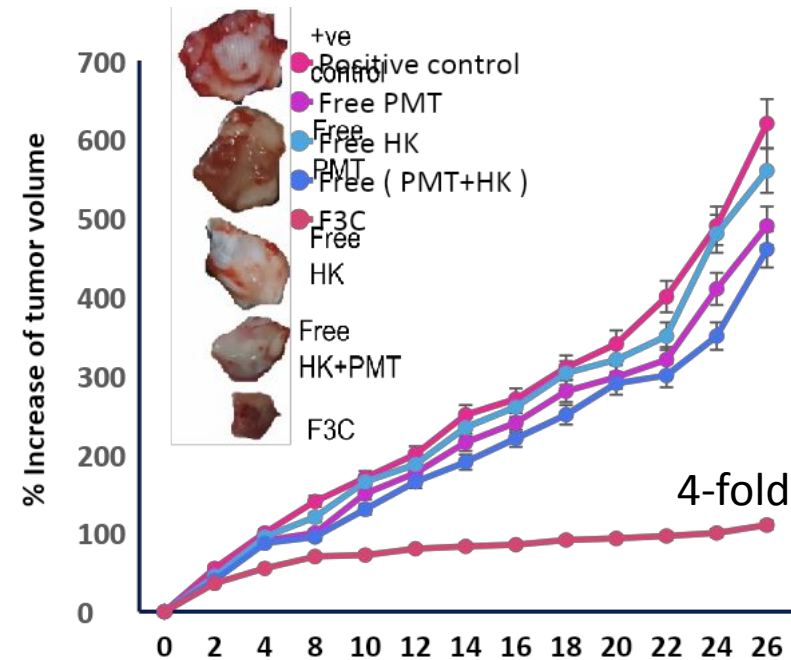
Positive control
Saline

Free HK

Free PMT

Free HK/PMT

F3C
PMT/HK
nanogel



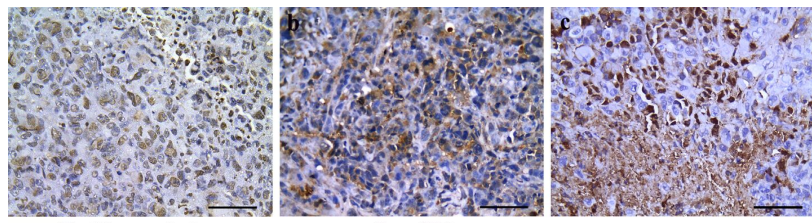
Time (Days)

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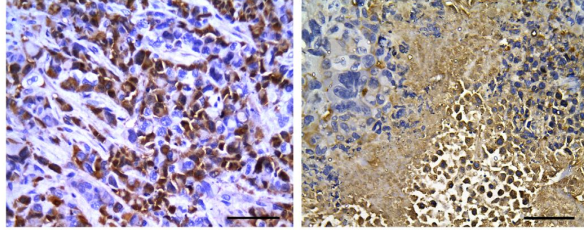
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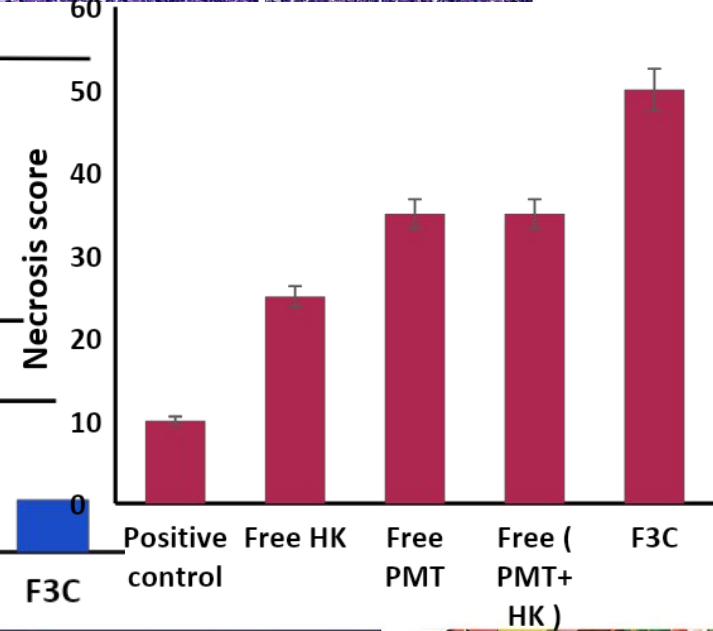
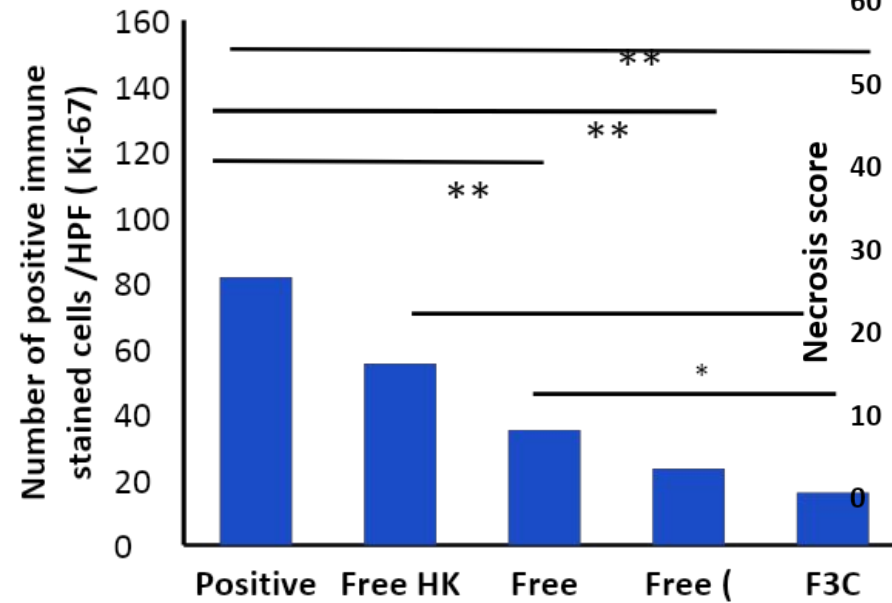
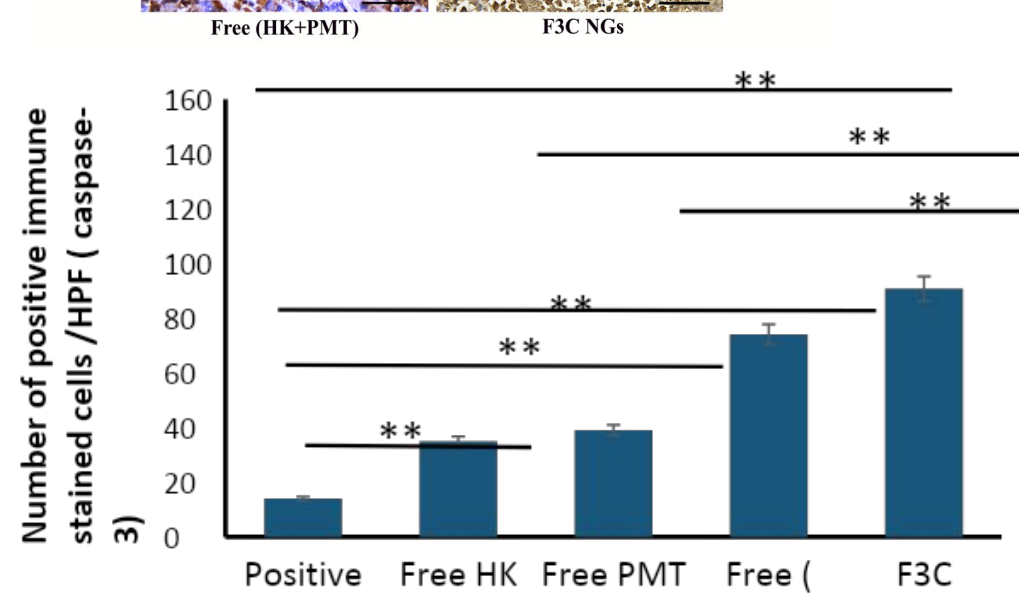
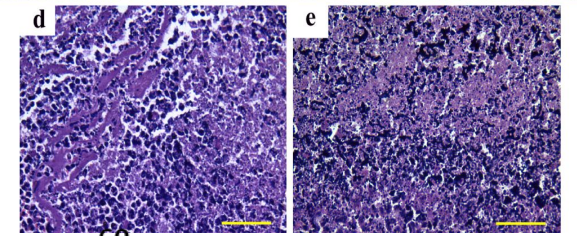
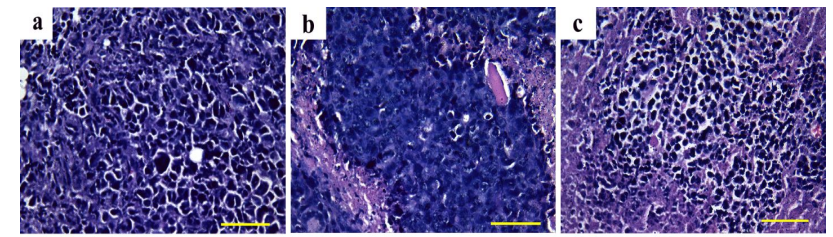
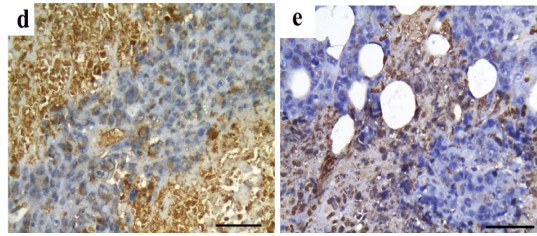
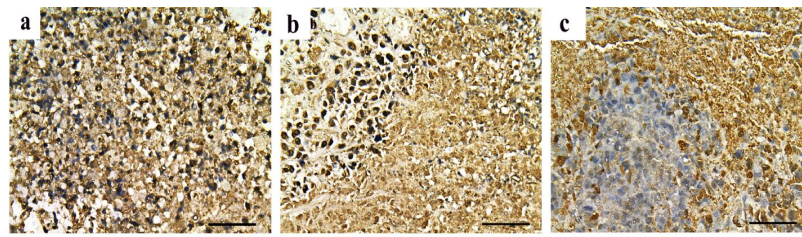
Immunohistochemical analysis



Positive control Free HK Free PMT



Free (HK+PMT) F3C NGs



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).

Breast cancer

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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