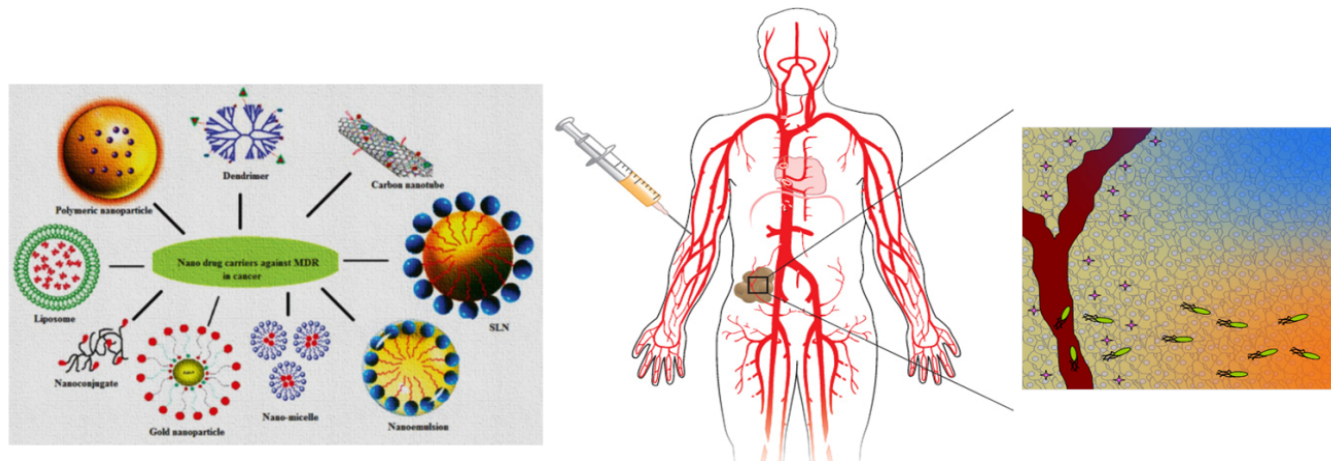


Improved chemotherapeutic efficacy against resistant human breast cancer cells with co-delivery of Docetaxel and Thymoquinone by Chitosan Grafted Lipid Nanocapsules



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Challenges with Docetaxel (DTX) based Breast Cancer Chemotherapy



Poor Biopharmaceutics properties



Dose related adverse effects; neutropenia, hypersensitivity reactions, hepatotoxicity, nephrotoxicity.



Non-specific tissue distribution



Development of Multi-Drug Resistance- Pgp mediated drug efflux.

Combination chemotherapy improving the cancer therapy

- ❑ Rationale strategy to increase response and tolerability and to decrease resistance



Major research interest

Combining anticancer drugs aiming at maximizing efficacy while minimizing systemic toxicity through the delivery of lower drug doses

NATURAL HERBAL MOLECULES

- ❑ Major players in pharmacology in general and in cancer research in particular
- ❑ New therapeutic approach as Combination chemotherapy
- ❑ Herbal natural molecule in combination with synthetic anti-cancer drug improve the cancer chemotherapy with reduction the toxicities
- ❑ Reduces the risk of recurrence and death

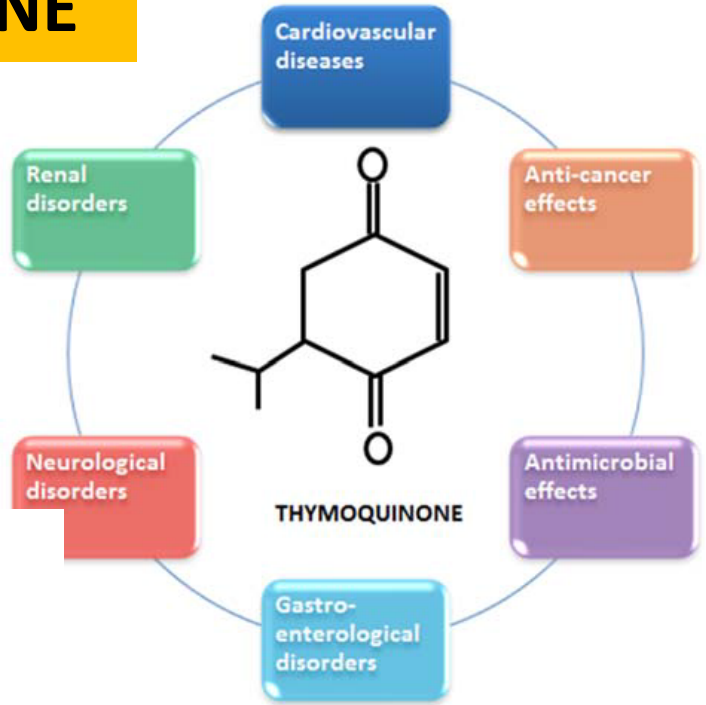
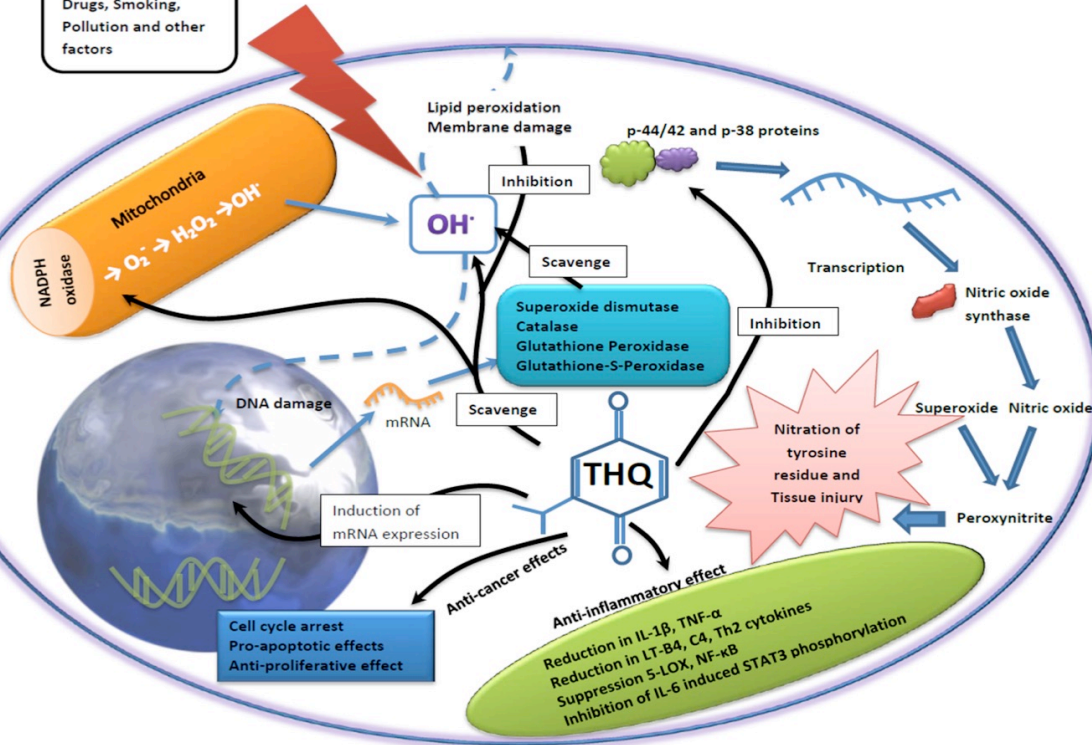
Delivery of combinational anti-cancer drugs in conventional formulation limit their optimal effect

THYMOQUINONE



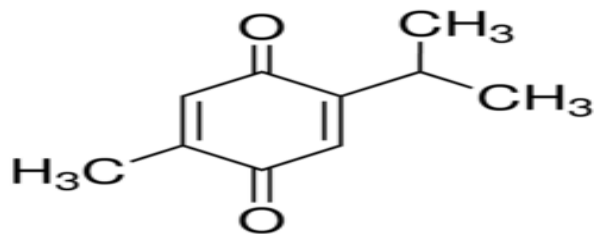
Black seed (*Nigella sativa*)

Ionizing Radiations,
Drugs, Smoking,
Pollution and other
factors



THYMOQUINONE

- Acts on multiple molecular targets in cancer cells via different pathways
- Exhibits anti-neoplastic and anti-angiogenic activity
- Hepatoprotective and neuroprotective



Nanocarrier based formulation of Thymoquinone improves oral delivery: Stability assessment, in vitro and in vivo studies

Anjali Singh, Iqbal Ahmad, Sohail Akhter, Gaurav K. Jain, Zeenat Iqbal, Sushama Talegaonkar, Farhan J. Ahmad*

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Supercritical anti-solvent technique assisted synthesis of thymoquinone liposomes for radioprotection: Formulation optimization, in-vitro and in-vivo studies

Iqbal Ahmad ^a ✉, Sohail Akhter ^{a, b} ✉, Mohammed Anwar ^a, Sobiya Zafar ^a, Rakesh Kumar Sharma ^c,
Arun Kumar Mishra ^d, Iqbal Ahmad ^{a, b} ✉

ARTIFICIAL CELLS, NANOMEDICINE, AND BIOTECHNOLOGY, 2018

<https://doi.org/10.1080/21691401.2018.1451873>

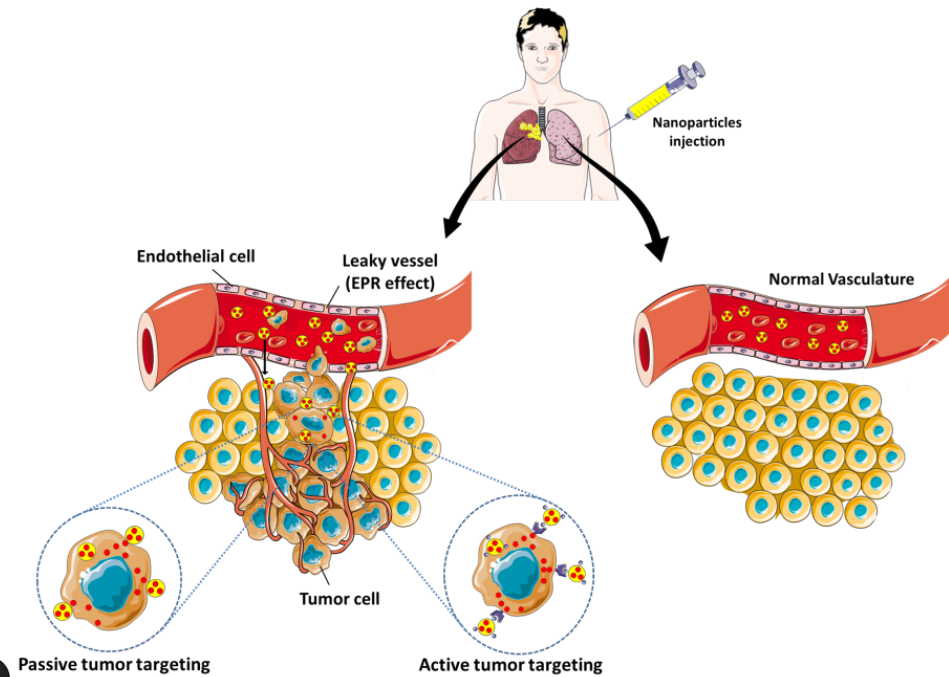
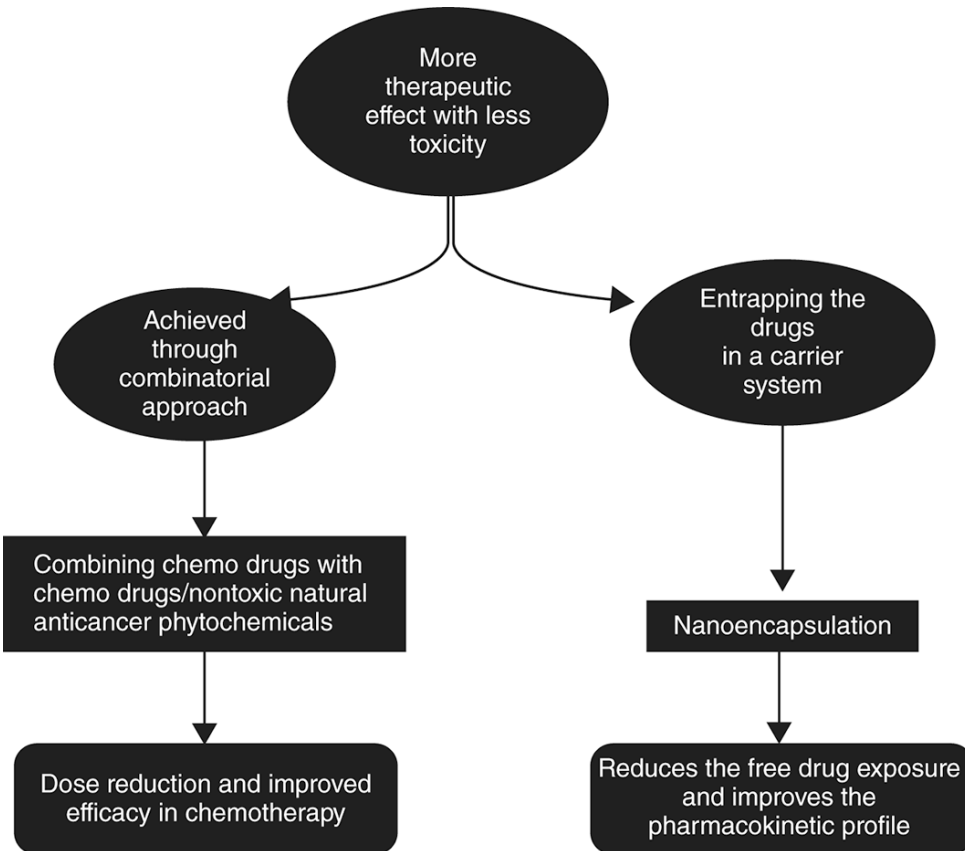


Formulation and evaluation of nano lipid formulation containing CNS acting drug: molecular docking, *in-vitro* assessment and bioactivity detail in rats

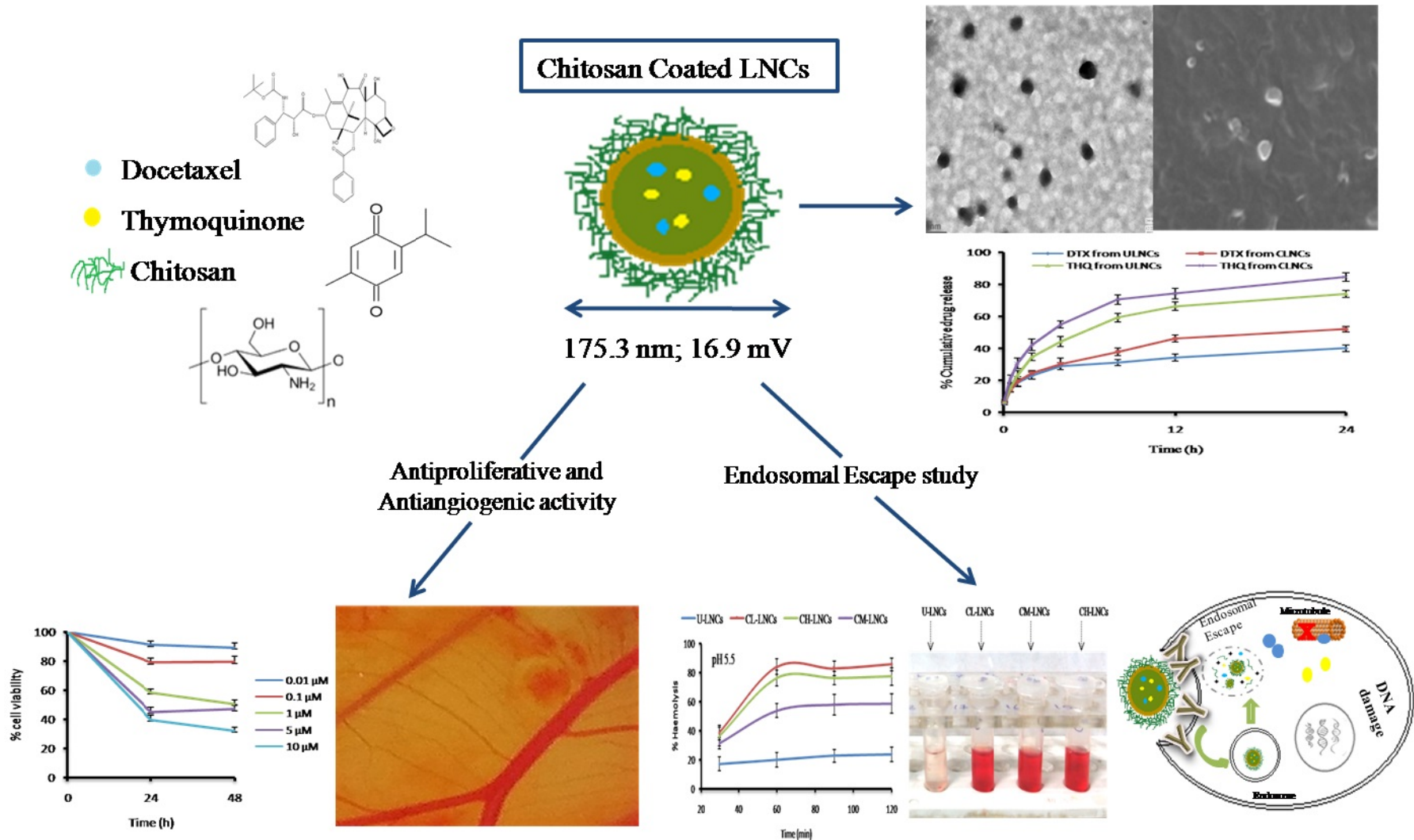
Mahtab Alam^a, Abul Kalam Najmi^a, Iqbal Ahmad^b, Farhan Jalees Ahmad^b, Md Jawaid Akhtar^c, Syed Sarim Imam^d and Mohd Akhtar^a

Combinatorial (synthetic and natural anti-cancer molecules) nanomedicines

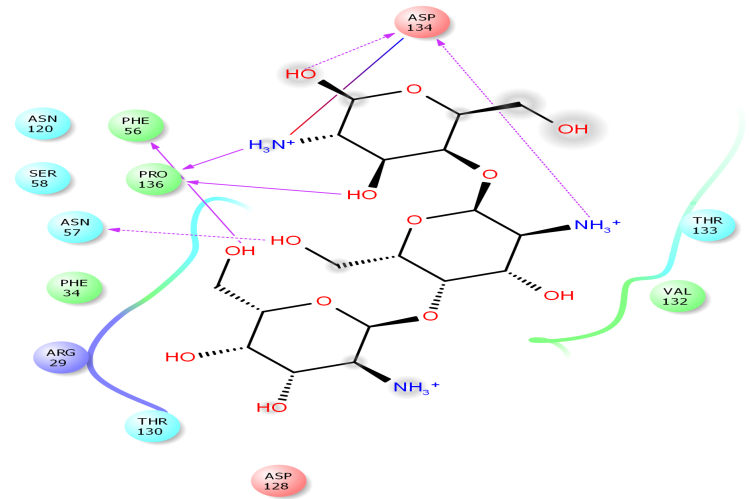
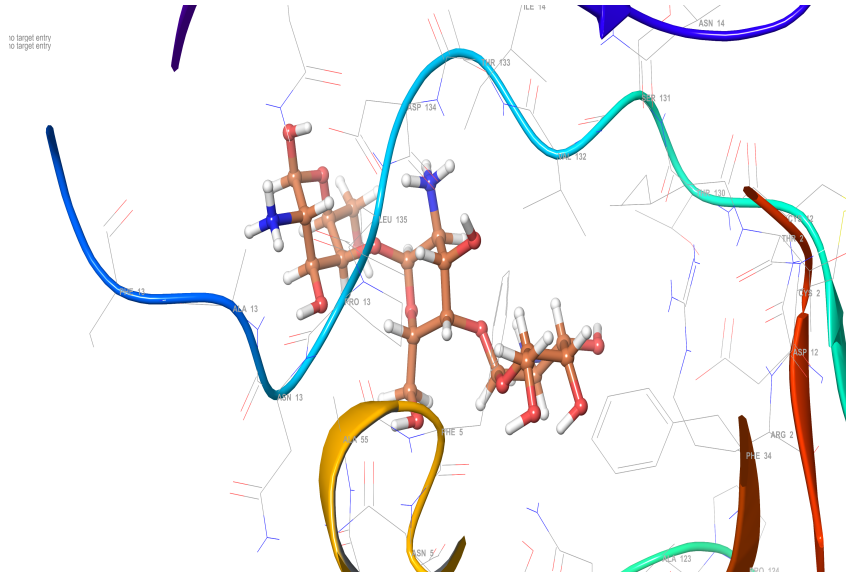
Nanomedicines



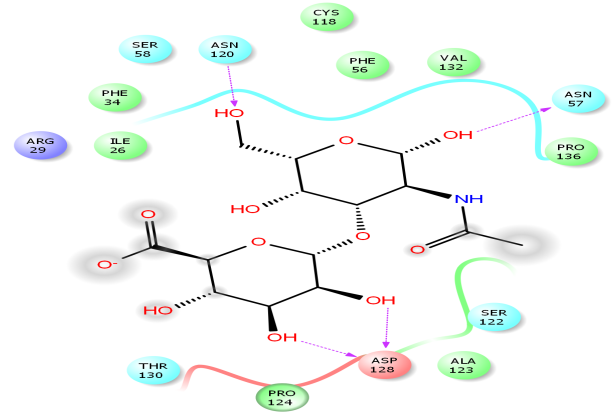
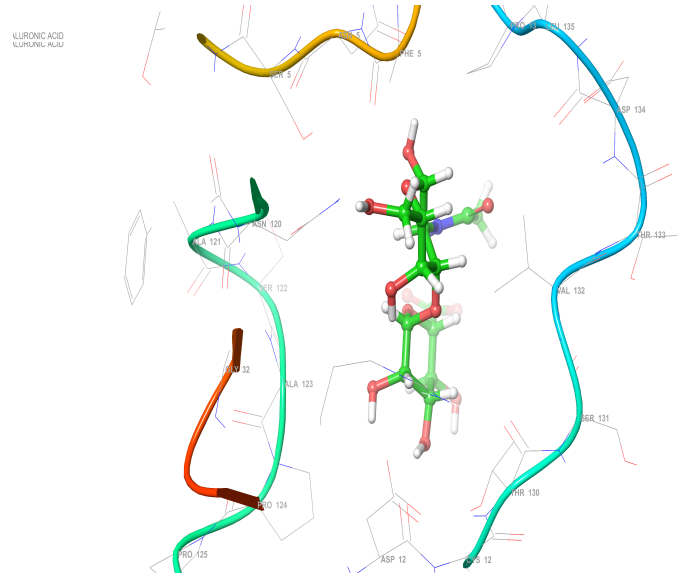
Improved chemotherapeutic efficacy against resistant human breast cancer cells with co-delivery of Docetaxel and Thymoquinone by Chitosan Grafted Lipid Nanocapsules



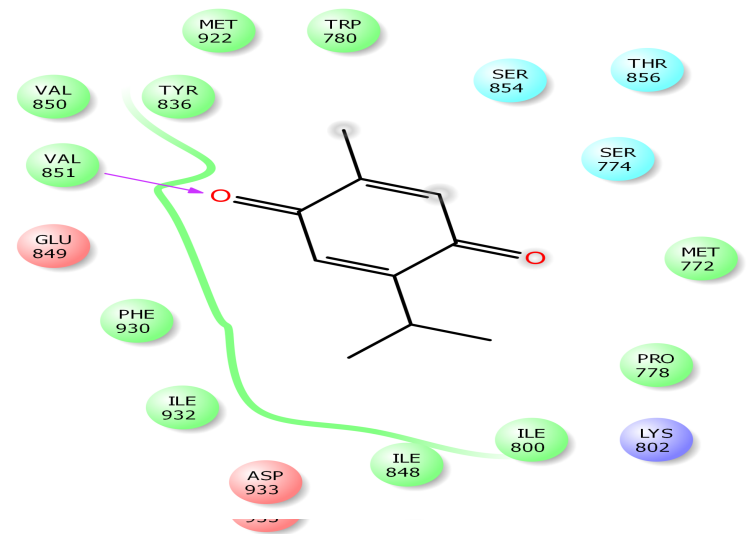
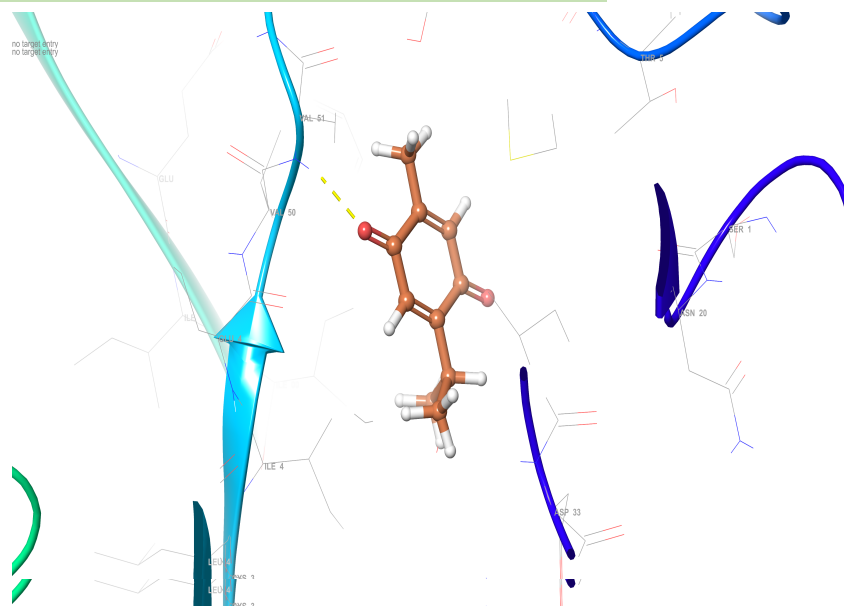
Chitosan-CD44 interaction



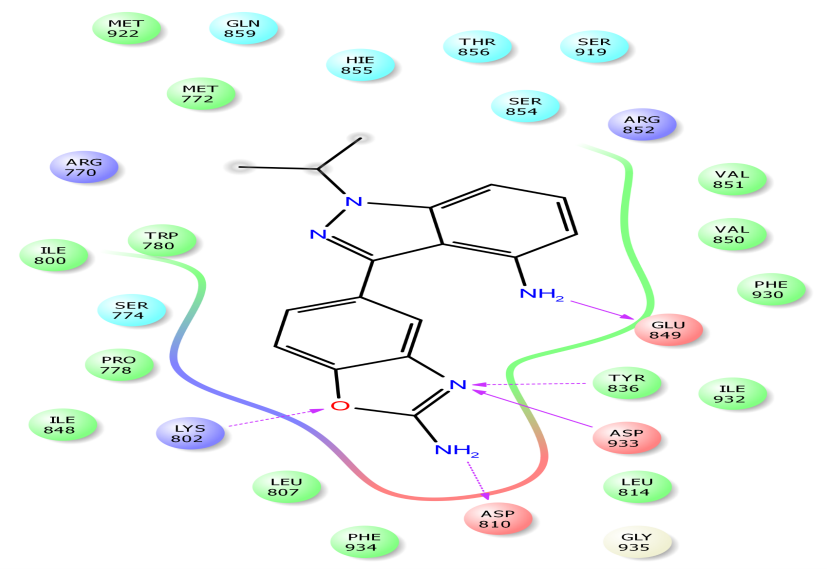
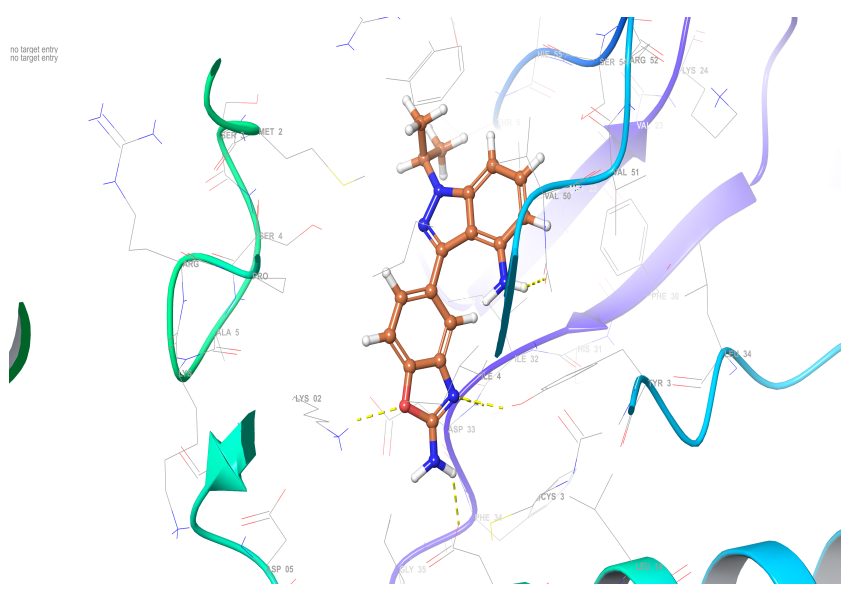
Hyaluronic acid-CD44 interaction



THQ-PI3K interaction



Standard-PI3K interaction



PDB ID	Receptor name	Ligand	Docking score	Glide energy
1UUH	CD44	Hyaluronic acid	-5.629	-37.604
		Chitosan	-6.922	-50.310
6GUF	PI3K	Thymoquinone	-7.170	-61.679
		Standard	-8.672	-72.586

Inference:

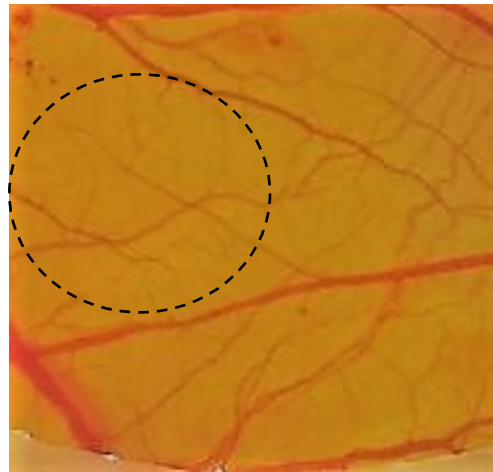
Docking score for chitosan was greater than that for HA which proved stronger interaction of Chitosan with CD44, crucial for active targeting.

THQ exhibited docking score closer to the standard PI3K inhibitor.

Angiogenesis Assay



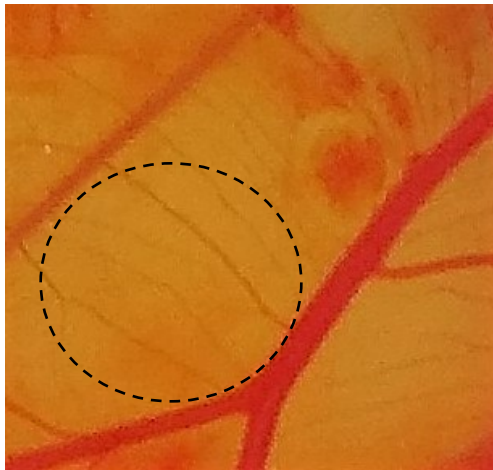
DTX



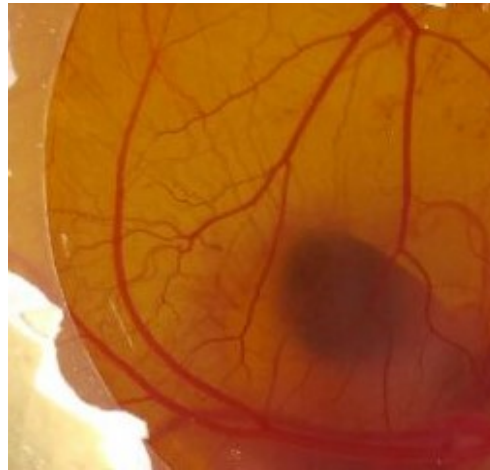
THQ



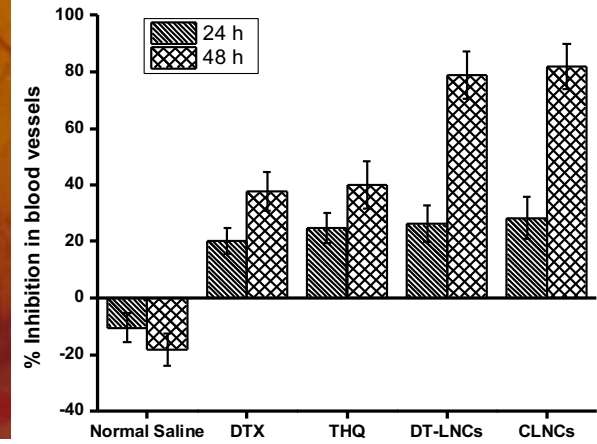
DxTq-LNCs



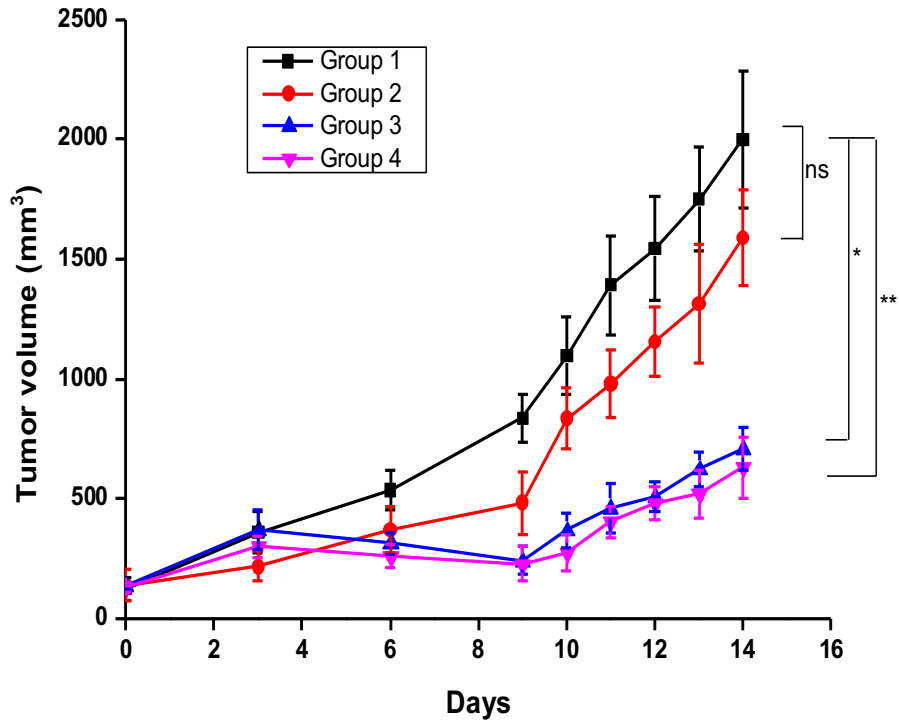
CLNCs



Normal Saline



Tumor volume estimation



Group 1



Group 2

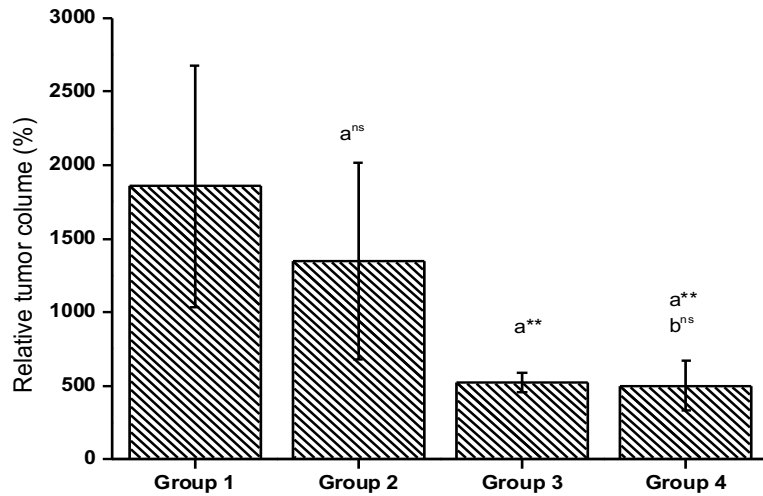


Group 4

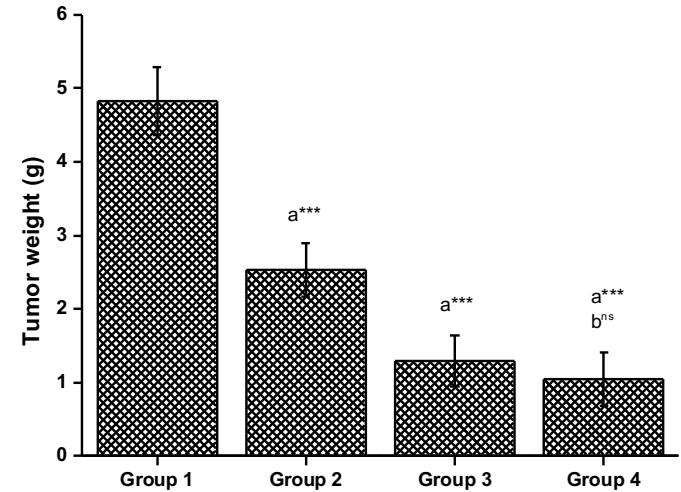


Group 3

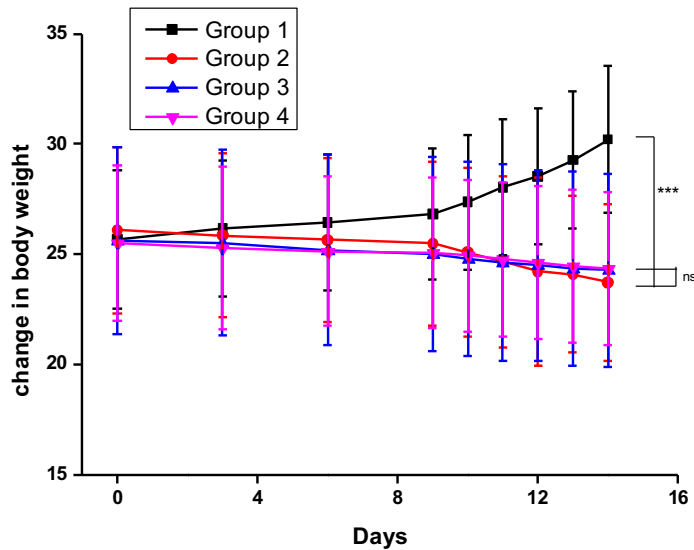
Change in Tumor volume



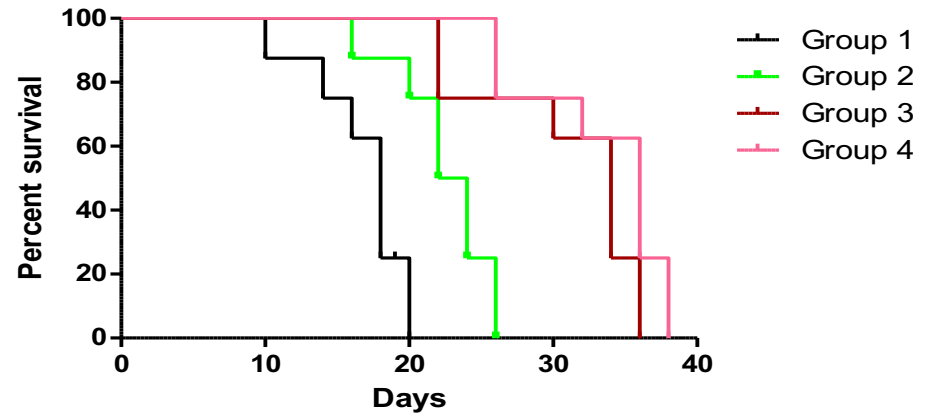
Tumor Weight at the end of study



Change in Body weight



Survival Analysis



	Control	DTX	DxTq-LNCs	CLNCs
Median survival time (days)	18	23	34	36

CONCLUSION

- Presence of THQ sensitized the resistant metastatic MDA-MB-231 cells to DTX treatment.
- Enhanced cytotoxic effects were observed with the CLNCs attributed to the CD44 targeting potential of Chitosan.
- The LNCs also demonstrated enhanced anti-angiogenic effect in the CAM assay.
- Collectively, dual drug loaded Lipid nanocapsules hold great promise for combined DTX/THQ chemotherapy to normal metastatic and resistant breast cancer with possibility of reduced drug dose, minimized side effects and maximized chemotherapeutic effect. The nanocapsules can serve as an effectual targeted chemotherapy and in parallel reduce the toxicity of DTX.

Journal Pre-proof

Improved chemotherapeutic efficacy against resistant human breast cancer cells with co-delivery of Docetaxel and Thymoquinone by Chitosan Grafted Lipid Nanocapsules: Formulation optimization, *in vitro* and *in vivo* studies

Sobiya Zafar, Sohail Akhter, Iqbal Ahmad, Zubair Hafeez, M. Moshahid Alam Rizvi, Gaurav Kumar Jain, Farhan Jalees Ahmad

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