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EFFECT OF THYMOQUINONE (TQ) NANOPARTICLE TO PROTECTIVE NEURO TOXCITY CELLS INDUCED BY EHRLICH ASCITES CARCINOMA (EAC) & LEAD IN VIVO STUDY

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ABSTRACT

This paper TQ-nanoparticle formulations showed improved anticancer and anti-inflammatory activities when compared with Cisplatin is a chemotherapy drug used to treat brain damage cancer. Here, we provide an overview of the various TQ-nanoparticle formulations, highlight their superior efficacy and discuss up-to-date solutions to further enhance TQ bioavailability and anticancer activity, thus improving potential for clinical translation.

KEYWORDS: Nanopartical, Thymoquinine (TQ), Cisplatin

Depration is the major cause of death and many factors that lead to its occurrences, such as environmental pollution and pesticide and other factors. Ehrlich carcinoma development depends on many things associated with the environment. The present study aimed to evaluate the potential protective effects of the active ingredient of Nagilla Sativa is a Thymoquinone (TQ). TQ nanoparticle research aims to improve TQ's pharmaceutical effects, such as targeting capacity, bioavailability, and avoiding unspecific binding. Different formulations of TQ nanoparticles were tested against several of brain damage & cancer, whereby the studies showed greater effectiveness of TQ nanoparticle than free TQ. These formulations included nanostructured lipid carriers (NLCs), solid lipid nanocarriers (SLNs), polymeric, niosomal, and liposomal. Using Nanopartical formulation, against Ehrlich ascites carcinoma (EAC) & lead-induced damage in the prefrontal cerebral cortex, hippocampus, and cerebellum can lead to a variety of neurological disorders, such as brain damage, mental retardation, behavioral problems, nerve damage, in male mice. Thymoquinine (TQ) is a promising anticancer molecule that inhibits cancer cell growth and progression in vitro experminal animal model. Despite the promising anticancer activities of TQ, its translation to the clinic is limited by its poor bioavailability and hydrophobicity. As such, we and others encapsulated TQ in nanoparticles to improve its delivery and limit undesirable cytotoxicity.

MATERIALS AND METHODS

The Ehrlich Tumor Cells Inoculation & Lead

The Ehrlich tumor cells were collected from ascitic fluid of the peritoneal cavity of mice 10 days after tumor administration. The ascitic fluid was washed in phosphate-buffered saline (PBS, pH 7.4), centrifuged (200 g, 10 min), and washed with PBS three times. The cell viability was determined by the 0.5% trypan blue exclusion method in the Neubauer chamber. The Ehrlich tumor cells were suspended to the final concentrations of 1 × 104, 1 × 105, 1 × 106, and 1 × 107 in 25 µL of saline. Measurements were performed before and after injection of tumor cells between days 0 and 12.

Dose of lead using by injection of 350 mg/kg lead

Protocols

Firstly, mice received intraplantar (i.pl.) injection of the Ehrlich tumor cells (1 × 104–107 in 25 µL) with 350 mg\kg of lead (mix) or saline. Measurements of mechanical and thermal hyperalgesia, paw edema/tumor growth, and overt pain-like behavior were performed on days 0–12. According to the results, the dose of 1 × 106/paw of tumor cells was chosen for next experiments of mechanical hyperalgesia, thermal hyperalgesia, paw edema/tumor growth, and histological analysis at indicated timepoints. The dose of 1 × 107/paw of tumor cells and evaluation at the 8th day after inoculation were chosen for experiments of overt pain.

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Paw samples were collected for histological analysis and microscopic observation 12 days after tumor injection. To evaluate the hyperalgesic effect of cellular remnants, the Ehrlich tumor cells with lead were inactivated and injected i.pl., and compared with the saline and the viable Ehrlich tumor cells groups; measurements were performed on days 0–12. To evaluate the pharmacological modulation of the Ehrlich tumor-induced pain-like behavior, mice were treated with Cisplatin 5mg\kg i.pl.injection and TQ-nanoparticle treatment orally administrated 10 mg\kg on the 8th day after the Ehrlich tumor cells & Lead administration.

Experimental Design

A total of 40 adult male Swiss albino mice was randomly assigned into 4 groups, 10 mice each. Control group: Mice were orally administered distilled water, day by day, till the end of the experiment. Lead & EAC (mix) group: Mice were injected (i.p) with 0.2 mL of 2.5 × 106 EAC cells & 350 mg\kg of lead mix /mouse on day “0”. Mix then TQ-nanoparticle protected group: Mice were orally administered distilled water, day by day, for two weeks before mix inoculation, and 3 days after mix inoculation; mice were orally treated with TQ nanoparticals (100 mg/kg), day by day, till the end of the experiment. Cis-treated (mix then Cis) group: Mice were orally administered distilled water, day by day, for two weeks before EAC inoculation, and 3 days after mix inoculation; mice were treated with a single i.p dose of Cis (5 mg/kg) day by day, till the end of the experiment.

RESULTS AND DISCUSSION

The current study proved the impairment of brain functions inmix of lead & EAC-bearing mice, which was indicated by the elevated serum dopamin & sertonine levels. In association with these findings, various vascular, degenerative, and inflammatory pathological changes, along with a heavy infiltration of neoplastic cells were also recorded in Brain tissue of EAC-lead -bearing mice., the elevation of brain function biomarkers could be attributed to the brain damage induced by the tumor metastasis and the infiltration of cancer cells in brain tissue, resulting in the impairment of the reduction in serum dopamin & sertonine Oxidative stress is well known to be one of the pivotal triggers for cancer initiation and progression, and it is also implicated as a possible mechanism of EAC-induced renal damage by asignificant evaluated serum dopamin & sertonine. Recorded brain oxidative damage, evidenced by a significant reductions in the GSH the precursor for tumor progression that ultimately decreases the cellular antioxidants and, subsequently, induces brain tissue damage the nanoTQ treatment is able to fix dopamine, serotonin unbalance In a record time during the period of neuro damage symptoms, which contributes to solving the problems and symptoms of Brain da symge symptoms and their complications.

Effect of Thymoquinone (TQ) nanoparticle on Ehrlich tumor cells induced tumor and inflammation on serum TNF-a levels in experimental rats. Statistical analysis was done by Prism software and graphs were automatically generated according to p value. * to **** indicate least to maximum significant difference (high to low p value). ns indicates non-significant values. Each value represents the mean± SEM of the group. Tumor with thymoquinine nanoparticles dose show significantly decreased TNF-a and significantly increase of GSH levels (Figure 1).

Effect of Thymoquinone (TQ) nanoparticle on induced neurotoxicity on serum dopamin & sertonine levels in experimental mice. Statistical analysis was done by Prism software and graphs were automatically generated according to p value. Results showing significantly balance of serum dopamin & sertonine level No siginficant correlation between Thymoquinone (TQ) nanoparticle group and Cisplatin treated groups.

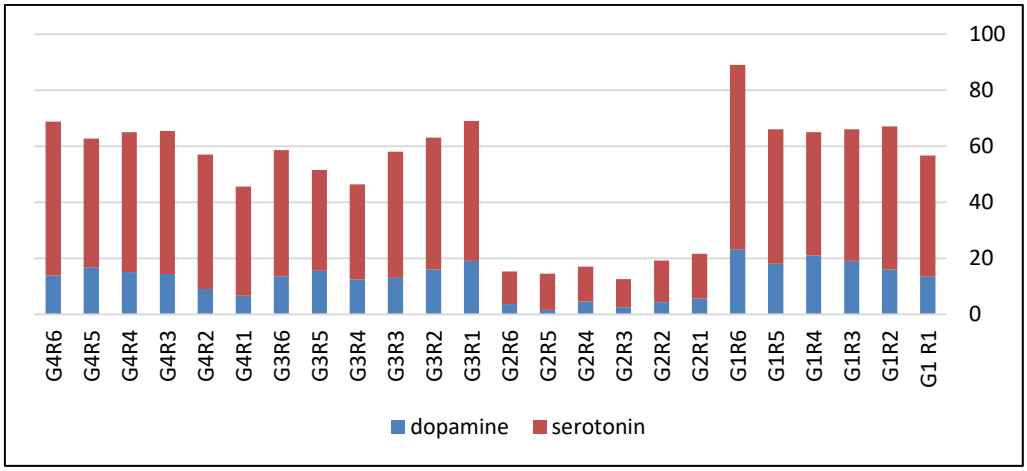

Figure 1: Effect of nano TQ in brain damage neurotransmitters

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