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REVIEW ARTICLE **OPEN ACCESS**

Cytotoxicity and Antioxidant activity of some (Ziziphus) plant parts: Review

Rahul A. Ahirrao*, Mohamme Rageeb Mohammed Usman1
Mahatma Gandhi Shikshan Mandal's Smt. Sharadchandrika Suresh Patil College of Pharmacy, Chopda, Maharashtra, India.

ABSTRACT
The plants that have many therapeutic compounds which yet to be found. The Rhamnaceae family includes Ziziphus mauritiana (ZM) and jujube (ZJ). Fruits are rich in protein, fats, fibers, carbohydrates, reducing sugars, and non-reducing sugars. The leaves include sterol, triterpenoids, cardiotonic glucosides, leucoanthocyanes, tannins, saponins, and holosides. Whereas alkaloids, flavonoids, glycosides, saponins, and volatile oil elements were identified in the root. The antioxidant implies free radical protection. Cell cytotoxicity and proliferation assays are typically utilized in drug research to scrutinize, if constitute influence cellular proliferation or have specific cytotoxic effects. This review will undergo the in vitro Brine shrimp mortality assay, MTT test, Allium Cepa model (ACM), and DPPH radical scavenging results of the cytotoxic and antioxidant effects of ZM and ZJ. extracts. as compared to the conventional medicine etoposide, ZM root (ZMR) extracts have active chemicals with dichloromethane extract cytotoxicity Artemia salina. The ZJ seed and pulp (ZJSP) extracts shown strong antioxidant activity; but did not to have significant cytotoxic impact on diverse cell lines. Whereas, pulp extract has better DPPH radical scavenging ability than seed extract. In numerous experiments, antioxidants activity was demonstrated in the ACM by boosting DNA repair and toxicity and suppressing root elongation with ZM leaf (ZML) extracts at increasing doses. ZMR and ZML are high in phenols, which can be used in nutraceuticals and anticancer component in medicines. Further, in silico activity of cancer receptor specific target identification, invivo and invitro models for active ingredients against cancer cells can be performed in the future.
Keywords: Antioxidant, Anticancer, Allium Cepa (ACM), Brine shrimp, Cytotoxicity, Ziziphus.

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INTRODUCTION

There are several plant species that have medicinal chemicals that have yet to be discovered. *Ziziphus mauritiana* and jujube are members of the Rhamnaceae family. *Ziziphus mauritiana* is civilized to near amount through his native diversity, although it is largely produced commercially in India, where it has garnered a lot of horticultural attention. There are 58 genera and about 900 species in the family. They are high in phenolic compounds. It is an evergreen tiny plant till approximate 15 m tall with 400 mm or more trunk thickness, a scattering peak, spines and many loose branches. Fruits include a high level of protein, lipids, fibres, carbs, reducing sugars, and non-reducing sugars. Triterpenes and triterpene saponins are necessary factors. Sterol, triterpenoids, cardiotonic glucosides, leucoanthocyanes, tannins, saponins, and holosides are also found in the leaves. The root included flavonoids, glycosides, alkaloids, saponins, and oil of mostly volatile components. Antioxidant means that substances, particularly those derived from nature, can give free radical protection. Cell cytotoxicity and proliferation tests are commonly used in drug research to determine, if a compound influences cellular proliferation or has particular cytotoxic effects. Screening medicinal plants for antioxidant and anticancer activities is critical. Anticancer, refrigerant, calming, pectoral, indigestion, styptic and energizer are all uses for dried fruits. They are supposed to purify the blood and recover ingestion. Roots can be useful to improve dyspepsia problems. Fevers have been treated using a decoction of the root. [1]. This review covers the results of the invitro Brine shrimp mortality assay, MTT test, Allium cepa model and DPPH radical scavenging for cytotoxic and antioxidant properties of Z. mauritian and Z. jujube extracts. Several invivo and invitro cytotoxicity and antioxidant models were reviewed. Moreover, various solvent extracts are used with *Ziziphus mauritiana* root (ZMR), *Ziziphus mauritiana* leaf (ZML), and Ziziphus jujube seed and pulp (ZJSP). Traditional medicine has a vital role in illness prevention, symptom management, and treatment. Plants are used to cure a variety of diseases, and traditional herbal remedies account for around 85% of basic healthcare treatments. [1][2]. Ancient remedy has been proficient for over three thousand years in the country like Sri Lanka.

Furthermore, documented information on herbals aids in improving understanding of certain therapeutic plants and techniques of being used. The majority of Sri Lankans rely on traditional remedies to meet their health-care needs. [3]

Taxonomical Classification:

- Kingdom: Plantae
- Subkingdom: Viridaeplantae
- Phylum: Tracheophyta
- Subphyllum: Euphyllophytina
- Division: Mangliophyta
- Subdivision: Angiosperm
- Class: Mangnoliopsida
- Subclass: Rosidae
- Belongs to Family: Rhamnaceae
- Subfamily: Asteroideae
- Plant belongs to Tribe: Paliureae
- Belongs to Order: Rosales
- Genus belongs to : *Zizyphus*
- Species belongs to : *Jujuba* [5] [6]

Vernacular Names:

- English: Beri, Ber, Baer, Bor, Baer, Chine Apple, Aprin, Chinese Apple, Collie Plum, Chinese Date, Crab-apple, Cottony Jujube, Indian Cherry, Indian Jujube, Spiny Jujube, Jujube.
- Tamil: Elanthai
- Marathi: Bor
- Arabic: Ber, Nabbak-El-Fil, Bor, Nobig
- Gujarati: Bordi
- Assamese: Bagari, Bogori
- Malayalam: Badatam, Parinthudar, Kolam, Elentha, Cherumali, Badari, Ilantha, Jujube
- Hindi: Ber
- Kannada: Yelchi
- Sanskrit: Ajapriya, Badara, Karkandhu [6]

Cytotoxicity test:

Brine shrimp lethality assay:

The lethality concentrations were utilized to determine cytotoxicity. Ten nauplii were placed in three different doses of the plant extract. Afterward 24 hours (1 day), the living brine shrimp larvae remained calculated and lethality was estimated by dividing total number quantity of nauplii remain by the total number of nauplii. Accordingly in this model, the extracts, portions and pure isolated chemicals remained often verified by lethality to brine shrimp larvae. Multiple toxicities were determined with several concentrations like 1, 10, 100 and then 1000 ppm in 10 mL salt-water solutions having 1% DMSO (v/v). Each test active ten nauplii as well as survivors were identified afterward 1 day. For every concentration, three at least replications were employed. Distilled water was utilized as a blank control. The chronic LC50, a measure of toxicity with used extracts, which was measured using the probit technique as the lethal concentration for 50% fatality afterward 1 day of introduction. For plant extracts, LC50 values over 1000 ppm were regarded as not active. The brine shrimp lethality assay (BSLA) is a basic with low-cost technique that is used to investigate the potency of phytochemicals found in various medicinal herbal extracts. Hence, results of the current investigation showed that the lethality's degree was inversely related to extract concentration. All of the shrimp in the control group survived after 24 hours of monitoring. Despite yet, peak mortalities were seen up to 1000 g/mL concentrations, while minimal mortalities were shown on 1 g/mL concentrations. Moreover, researchers observed that at larger concentrations of the investigational extracts, the shrimps began to die mostly afterward 480 minutes and perished completely later 1 day (24 hours). Using probit analysis, the lethality (LC50) concentration was estimated. The regression line that resulted from graphing the concentration verses the death proportion with the probit scale was used to derive of LC50 (median lethal concentrations) values. [7] [8] [9] [10] [11]

The MTT test:

By transforming tetrazole yellow, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (M.T.T.), and purple formazan in live tissues, this test is often used to assess cell viability. Numerous cytotoxicity of the Jujube pulp as well as its seed extracts was evaluated using the MTT assay. Many cell lines were employed for this, including MCF-7, DU-145, C26, PC3, Hella, PCL12, A2780, and HTC. Entirely of the test

cells onto 96-well plates were seeded, which were at that time incubated at 37°C for 24 hours. The extracts were then added to plates and cultured for another 24 hours. The next step involved replacing the previous medium with one which contained MTT reagent and hatching it at 37°C about 180 minutes. Following removal of the medium, the plates were shaken, later DMSO was added upto 0.2 ml for dissolving crystals of formazan, and then plates were properly rinsed with phosphate-buffered saline (PBS). At 550 nm, the absorbance was measured. Soft tools calculated the cytotoxicity values. [11]

Model of Allium cepa:

For identification of change in cytotoxicity, genotoxicity, the mitotic index, chromosomal alteration, the root length was measured. Every one of the extracts investigated, the results demonstrated a shrinkage in the percentage mitotic index and a dose related reduction in root tip elongation change with a rise in extract concentration, with that of ethanol extract exhibiting positive extreme impact on mitotic index. Also, the effective concentrations of extracts (EC_{50}) for the aqueous, ethanol, ethyl acetate and hexane were 81.30, 52.01, 90.68, and 112.30 mg/l, respectively. In addition, chromosomal defects such travelling chromosomes, c-mitosis, bridging the anaphase, and humid telophase were found in all four extracts, and it was shown that the percentage of these aberrations decreased with extract concentration. [13] [14]

Antioxidant activity:

In this model, the promising cytotoxic as well as genotoxic effects of the various solvent extracts are determined by analysing mitotic index with its percentage, inhibition of growth of roots ends, amount or percentage of concentration, and root cell structure. Subsequently chronic treatment of 400 mg/kg of *Z. mauritiana* for about 42 days with rats, so antioxidant parameters including superoxide dismutase, total antioxidant capacity and malondialdehyde levels were determined into plasma consequently. [11]

CONCLUSION

Considering ZMR extracts to the conventional medicine etoposide, the order of dichloromethane, methanolic, and dichloromethane extract cytotoxicity against Artemia salina decreases. After receiving ZMR orally for six weeks, the levels of MDA in the plasma were lower and the levels of superoxide dismutase and total antioxidant capacity were higher as compared to that group of control, demonstrating the antioxidant and liver-protective benefits of ZMR. *Ziziphus mauritiana* seed and pulp (ZMSP) extracts had strong antioxidant activity, although an MTT test revealed that not a single tested extracts had a significant cytotoxic outcome on any of those tested cell lines. [14] *Ziziphus mauritiana's* roots and leaves are a rich source of phenolic composites, which may also be used as a component of medicines and nutraceuticals that fight cancer. [12] Root growth inhibition and the effective concentration in the Allium cepa model have significantly decreased when compared to the control, and extract concentrations have also risen. The ethanol extract's greatest growth inhibition. By using this approach, it was discovered that chromosomal abnormality % decreased together with the mitotic index. [14] *Ziziphus mauritiana* root (ZMR) extracts have active compounds with dichloromethane extract cytotoxicity along with Artemia salina as compared to the common medication etoposide. Although the Ziziphus jujube seed and pulp (ZJSP) extracts had considerable antioxidant activity, they had little to no cytotoxic effect on a range of cell lines. However, pulp extract is more effective in scavenging DPPH radicals than seed extract. Using *Ziziphus mauritiana* leaf (ZML) extracts at increasing concentrations, antioxidant activity was consistently demonstrated in the Allium cepa model by facilitating DNA repair and toxicity and preventing root elongation. The root and leaves of *Ziziphus mauritiana* are rich in phenolic composites, which are employed in nutraceuticals and as an anticancer ingredient in pharmaceuticals. [16] Further, in silico activity of cancer receptor specific target identification, *in vivo* and invitro models for active ingredients against cancer cells can be performed in the future.

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Author's Contribution

Rahul A. Ahirrao was the supervisor, designer of the hypotheses, and responsible for all the steps and wrote the text of the article.

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