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Review

A review on Citrulluscolocynthis plant and human poisoning

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Citrulluscolocynthis (L.) Schrad. is commonly known as colocynth. The fruit pulp of colocynth has medicinal properties while the seeds have nutritive qualities. C. colosynthis is resistant to high temperatures and grows in the desert regions of North Africa, the Middle East and Western Asia. C. colocyn this likely carries genes of interest that could be explored for inducing antibiotic resistance in transgenic plants. Although the tissue culture and molecular biology of this species have been explored, the latter has been primarily used to resolve taxonomic relationships with other members of the Citrulluscurcub its genus.

Keywords: Citrulluscolocynthis, plant and human poisoning.

INTRODUCTION

Medicinal plants are one of the most valuable resources in a wide range of Iranian natural resources that can play an important role in the health, employment, and non-oil exports if they are scientifically recognized, cultivated, developed and exploited.

In our country, the existence of low habitats, low dispersal and density, high traditional use and the role of these plants in the rural household economy have led to irregular consumption and unnatural harvesting of medicinal plants.

Citrulluscolocyn this is a one-year-old plant of the Cucurbitaceae family that grows mainly in arid and desert areas.

It is native to the warm regions of Asia (Syria), North Africa (Egypt) and the Mediterranean coast.

In Iran, you also go wild in the south of Kerman province (Jiroft city), Fars province (Kazeroon city), Sistan and Baluchestan province, Hormozgan, Yazd and Khorasan provinces (Safavi, 2011).

The fruit and seeds of this plant have been used to treat constipation, bowel weakness, headache relief and joint pain (Mirheidar, 1996).It is now being used to treat diabetes and prevent cancer cells from growing. In addition, the fruit of this plant also has antimicrobial properties (Gurudeeban, 2011).

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In terms of chemical constituents, the fruit of this plant has two types of glucosides, namely clucentin and cucurbitacin. Cloacetin is a highly toxic and bitter biochemical compound that is mainly found in the Abu Jahl watermelon plant and in all its parts.Cucurbitacin is also a bitter biochemical substance found in the fruits and roots of some Cucurbitaceae family plants and is produced to protect the plant against vegetarians. These two compounds form the bulk of the plant's active ingredients. (Mirheidar, 1996).

Chemical Composition

The seeds are rich offatty acids such as myristic, palmitic, stearic, oleic, linoleic and Linolenic acid. It is reported that the de-oiled cake can be incorporated in the cattle feed of milking cows up to 25% and it did not exhibit significant effect on the milk yield (Khatri *et al*., 1993). Tumba seed oil is edible; its composition is similar to soybean oil. Refining and washing with citric acid removes it's bitter taste (Ramakrishna *et al*., 1993).

Akhtar *et al*. (1999) reported that during germination of seeds in the dark at 30°C, the relative amounts of triacyl glycerol decreased, while the free fatty acids increased continuously in significant amounts. However, it was mentioned that saturated fatty acids are increased and unsaturated fatty acids decreased gradually during germination.

The protein content of seeds of colocyn this (transitional weed) was found to be 8.25% and rich in lysine, leucine and sulfo-amino acids viz., methionine. (Shaheen *et al*., 2003). Egusi (colocynthis) kernels contain oil (52%), protein (28.4%), fiber (2.7%), ash (3.6%) and carbohydrate (8.2%). These are good sources of essential amino acids (such as arginine, tryptophan and methionine) and vitamins (B1, B2, Niacin) and Minerals (Ca, Mg, Mn, K, P, Fe and Zn) . Flavonoid quercetin was isolated from *in vivo* (leaf, stem, fruit and root) and *in vitro* callus of the species (Meena and Patni, 2008). Estimating the protein and amino acids composition of defatted seed meal showed high protein content (40.5%) and it was reported that the essential amino acid tryptophan is absent.

Flavone c-glucosides were identified in fruits and aerial parts of *Citrulluscolocynthis*. Fruit contains iso-vitexin, iso-orientin and iso-orientin 3'-methylether, while the aerial parts contain three C-p-hydroxy benzyl derivatives viz., 8-C-p-hydroxybenzylisovitexin, 6-C-p-hydroxybenzylvitexin and 8-C-p hydroxybenzylisovitexin 4'-O-glucoside (Maatooq *et al*., 1997). The lipase and phospholipase extracted from the meal of mature seeds of *C. colocynthis* showed an optimum activity at 40°C and pH 7 in aqueous media. n-heptane was found to be the most suitable solvent medium to obtain maximum activity from these enzymes. The activity of lipase extracted from germinated seeds increases with the stage of growth. However, the activity of phospholipase decreases with increase in size of the seeds (Akhtar *et al*., 1999).

Fruits of *Citrulluscolocynthis* contains seventeen compounds were broadly identified and divided into five classes *viz*., alcohols, ketones, epoxy compounds, hydrocarbons and an acid. The alcohols identified were 4-(1-methyl) ethoxy, 1-Butanol; 5-methoxy, 2-methyl, 2-pentanol; 1-cyclopentyl, 2-propene-1-ol and 2-Furanmethanol, tetrahydro-5-methyl-*cis* and *trans* isomers. Ketones were including 3, 4-Dimethyl, 2-hexanone; 2-Methyl, 4-heptanone and 3-Methyl, 2-heptanone. Two epoxy compounds were 1-propoxy pentane and 2, 3-epoxy methyl propionate and palmitic acid. Four hydrocarbons maybe present on the surface of the fruit in minimum quantities were including tridecane, tetradecane, pentadecane and hexadecane. The two remaining compounds are (viz., Trimethylsilylmethanol) impurity component derived from silicone oil used in the isolation process and the other impurity (viz., 1, 2-benzenedicarboxylicacid, diisooctylester) was stabilizer for plastics (Gurudeeban, 2007). All these compounds must have been derived by fatty acid pathway.

Pharmacological Studies

Antimicrobial activity: *In vitro* antimicrobial activity was examined for aqueous and methanol extracts of *Citrulluscolocynthis*. Antibiotic sensitivity of strains was determined by the standard Disc diffusion method (Bauer *et al*., 1960) against a number of antibiotics including two antifungal drugs. The agar disc diffusion method was followed for antibacterial susceptibility test. As a result of this study, the aqueous extract showed high antibacterial activity against *E. coli* and *Staphylococcus aureus*but considerably less effect against *Klebseilla pneumoniae* and *Bacillus subtillus* and on the other hand the aqueous extracts did not exhibit any antibacterial activity. It should be noted that methanol extracts of the plant showed high antibacterial activity against *Bacillus subtillis*, *Streptococcus pyogenes, Salmonella typhi* but considerably less activity against *Streptococcus faecalis* and on the other hand showed no effect against *Proteus mirabilis*, *Proteus vulgaris* and *Vibirocholerae*.

Ethanol extracts of fruits, leaves, stem and roots were found to be active against Gram positive bacilli, viz., *Bacillus pumilus* and *Staphylococcus auerus*, while fruit and root extracts in double strength gave positive results against gram positive Bacillus subtilis. The gram negative bacilli viz., *Escherichia coli* and *Pseudomonas aeruginosac* showed no response (Memon *et al*., 2003). Antifungal activity was determined against six fungi. The stock culture was maintained in Glucose Peptone Yeast and Sucrose (GYPS) medium. The methanolic extract of the plant showed high antifungal activity against *Aspergillus fumigatus*, *Mucor* sp. and *Aspergillus flavus, Candida*

albicans, Pencillium sp. and *Rhizopus* sp. did not show any antifungal activity (Gurudeeban *et al*., 2010).

Anti-cancer activity of Abu Jahlwatermelon: Cancer begins by escaping a cell from the natural barriers to cell proliferation and proliferating without control (Jena et al., 2012).According to the International Agency for Research on Cancer Research, lung cancer is the most common type of cancer with 13%, followed by breast cancer with 11.9%, colon cancer with 9.7% and prostate with 7.9% the most common types of cancer In the world (IARC, 2014).In Iran, the average incidence of cancer is134.7 per 100,000 people and 55,000 per year die from cancer (Asadi-Samani, 2015). Despite many advances in cancer treatment, there is a need for the discovery and introduction of new and alternative drugs due to the emergence of mammalian tumor cells to chemotherapy and its many side effects (Harlev et al., 2012).

There is extensive documentation on the preventive properties of various types of herbs that are consumed as food, fruits, spices, and vegetables against cancer (Moyad et al., 2004).

In the Afshari relay study, the results for Hep2 cell line showed that at the highest concentration (100 µg / ml) of the plant extract, the cell growth was completely inhibited. This effect was reduced by decreasing the concentrations of extract (0.025 µg / ml, 0.25, 2.5, 25, 50) IC50 was obtained for 27 µg / ml Hep2 cell line. Morphological and cellular proliferation results of Ab-Jahl watermelon extract on normal mouse L929 cell line showed no cytotoxicity (Tavakol Afshari 2005).

The study of Gupta was performed to evaluate the anti cancer activity of Citrulluscolocyn this Linn. fruit extract. Cancer was induced in experimental Swiss albino mice by introduction of Dalton ascites lymphoma (DAL) cells intraperitonealy (i.p). The above cancerous agent brought abnormalities in levels of RBC (red blood cells), WBC (white blood cells), SGPT (serum glutamic pyruvic transaminase), SGOT (serum glutamic oxaloacetic transaminase), GSH (glutathione), CAT (catalase), SOD (superoxide dismutase) and tumor volume. These parameters were statistically improved by our extract, which Might be because of the presence of numerous phytoconstituents present in the extract, it is showing anti cancer activity by virtue of antioxidant, free radical scavenging and tumor cytotoxicity activities. (Gupta et al., 2019).

The study of Rezai was investigate the anti-proliferative and cytotoxic activity of the hydro-alcoholic extracts of Citrulluscolocynthis (L.) Schrad on the AGS and MCF-7 cell lines. After preparation extracts by maceration procedure, different concentrations (control, 0.001, 0.01, 0.1 and 1 mg/ml) of C. colocynthis (L.) Schrad fruit extracts were added to cell lines and incubated for 24, 48 and 72 h. The viability of cells was evaluated by MTT Assay. Then optical density of each cell was readied by ELISA at 570 nm. Our results showed that hydro alcoholic extracts of C. colocynthis (L.) Schrad had significant anti-proliferative effect on MCF7 and AGS cell lines. Data analysis was showed that there were significant differences in cell viability after 24, 48 and 72 h. These differences were showed in 72h a dose-dependent approach (Rezai et al., 2017).

The cucurbitacin glycoside from *Citrulluscolocynthis* leaves was examined for anticancer us effect in human breast cancer cellproliferation. The glycoside in the combination of1:1 inhibited multiplication of ER- MDA-MB-231and ER+ MCF-7 human breast cancer cell lines.The cell-cycle study showed that therapy with

screened cucurbitacin glycoside combination emerged in growth of cells at the G2/M stage of the cycle. Evaluated cells showed an acceleratteddecline in the production of the protein complex necessary to the management of G2 exit and beginning of mitosis, specifically the p34CDC2/cyclin B1 complex. This showed that cucurbitacin glycosides show signs of pleiotropic effects on cells, provoking both cell cycle arrestand apoptosis, it means cucurbitacin glycosidesmight have beneficial significance against cancer cells [Al-Snafi, 2016]. Anti-cancer effect of alkaloid rich extract of *Citrulluscolocynthis* fruits was explored. The cytotoxic effects were evaluated onMCF-7 cells showed significant reduction in cellactivity in dose dependent approach (LC50=17.2µg/mL) at very small concentrations such as 5, 10 and20 µg/mL [Daoudi, 2013]. The cytotoxic effect of the crude extract of *Citrullus Colocynthis* and TiO2nanoparticles (NPs) was examined individuallyon cancer lines and recombinant mouseepithelial cell line on the surface of cells incomparison of the combination of both. Theresults revealed that the plant extract and thenanoparticles alone showed significant reductionin the growth of cell line instead of theircombination, the combination exhibitedantagonistic effect [Upadhyay, 2007]. The cytotoxic study of four plants *Aristolochia longa* (L), *Citrulluscolocynthis* (L), *Piper cubeba* (L) and *Delphinium*

Staphisagria (L) was examined on five differentcancer cell lines MCF7, HT29, N2A, H5-6 andVCREMS with 3-(4,5-Dimethylthiazol-2-yl)-2,5-

diphenyltetrazolium bromide (MTT) assay at adose of 500 µg/ml. *P. cubeba* (L) concentrate showed the prohibition of 98.64 and 91.59% and*C. Colocynthis* (L), 91.84 and 85.58% againstMCF7 lines and HT29 cell lines, respectively.

C. colocynthis (L) exhibited a dose-dependent effect on the respective cell lines with an IC50 of22.0 and 32.5 µg/ml [Shawky, 2014].

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