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RICINUS COMMUNIS L – A MEDICINAL PLANT POTENTIALLY HARMFUL TO HUMAN HEALTH

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ABSTRACT

Since ancient times, humans learned that some herbs prevent or even heal various medical conditions, regarding the fact they are a valuable source of bioactive substances that contribute to a good health state. The use of medicinal plants takes causion because some species contain several toxic metabolites, as well. Among the phytotherapeutic herbs, a well-known plant is *Ricinus communis* L. The extracts from the various vegetative organs have many medicinal effects, whereas the castor beans (the seeds) are considered harmful to the human health. They contain a natural toxin, named ricin, that may cause severe or even lethal effects if it reaches inside a human or animal living organism. This scientific contribution is based on relevant published literature in this field. The paper aims to enhance both aspects in *Ricinus communis* L.: its importance as a medicinal species, and the danger it represents due to the high toxicity of its seeds' ricin. People should be aware of the antagonistic effects of this plant, mainly in this specific context, in which herbs and their seeds are increasingly used for therapeutic purposes or as a dietary source of natural fats, proteins, fibers, vitamins, minerals, and other biologically active substances.

INTRODUCTION

Since ancient times, humans discovered the use of herbs for food, and to prevent or cure various medical conditions, due to their active principles. These active compounds are metabolic derivates deposited in various vegetative organs, such as: leaves, roots, seeds, bark etc. (Munteanu, 2014). The natural substances are endowed with specific characteristics that vary from the synthetic conventional molecules used in the drug medication manufacturing, structurally improved by evolution, in view of maintaining various biologic roles, including the optimization of the inner defense mechanisms (Atanasov et al., 2021).

There has been noticed an increasing zest for the phytotherapeutical products in the last few years. Nevertheless, along with their therapeutical effects, some vegetal products may be toxic. The phytochemical content should be assessed and taken into consideration, along with the awareness on the side effects (Capasso et al., 2000). There has been an outburst of scientific papers issued on the topics of phytomedicine and ethnopharmacology, showing a growing interest in plant medicine, and in elucidating their intricated roles, paths and possible toxic effects (Panossian, 2023).

The awareness and the identification of the toxic compounds, harmful to the human health, is essential for the safe use of medicinal plants, along with their herbal extracts or products. The occurrence of the accidental intoxications must be prevented. The research of the plant toxicology and how herbs interact with the human organism may facilitate the development of some risk assessment methods regarding the use of plants and their derivatives, and how they affect human health (Wu et al., 2011).

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1. The therapeutic and economic relevance of *Ricinus communis* L. species

Ricinus communis L. (the castor bean or castor oil plant) is a species of perrenial flowering plant in the *Euphorbiaceae* family. The particular leaf shape lead to the common names, such as: *Christuspalme* (the palm of Christ), *Kreuzbaum* (the cross' tree), or *Wunderbaum* (the wonder tree). The species originates in Africa. It was used by the Greeks and by the Romans for its medicinal purposes in Ancient Egypt (Worbs et al., 2011). The species grows in the wild in many tropical and subtropical regions, but may be encountered as an ornamental plant almost all over the world.

Several vegetal organs and the oil are widely used as traditional valuable medicines for thousands of years. The castor oil plants comprise a wide range of valuable phytochemical compounds, used as: antioxidant, anticarcinogenic, antiinflammatory, antiasthmatic, analgesic, antidiabetic, antimicrobial, antiviral, and as a remedy for the wound healing (Yousefsani et al., 2024).

The ethanolic root extract is a very efficient antiasthmatic, antihistaminic, and it regulates the mastocytes' activity. The medical conditions caused by the oxydative stress may be cured using the castor beans extracts. The leaves' chemical compounds are immunomodulators, they increase the phagocytic activity of the human neutrophils, (Mishra et al., 2022). The previous examples are merely a fraction of a multitude of beneficial effects described by the scientific papers on the therapeutic use of *Ricinus communis* plants.

The chemical composition of the castor oil is rich in fatty acids; the most valuable is the ricinoleic acid, that represents about 75 - 90% of the total amount of seed - extracted oil. There were evinced some neutral fats (triglycerides), as well, and several biologically active compounds in small amounts (carotenoids, phenols, phospholipids, phytosterols, tocopherols, tocotrienols), (Yeboah et al., 2021). The castor oil is therapeutically used as: laxative, antimicrobial, and antiinflammatory. Its analgesic effects recommend its use to alleviate muscle and joint pain. Its active compounds may have a calming effect, reducing the discomfort caused by these painful medical conditions. The topic use of castor oil relies on its emollient, nourishing, and moisturising effects. The oil can be applied on the skin to keep the moisture, soothen irritations and minor inflammations. Due to these roles, the castor oil is frequently a part of the formula for various cosmetics, skin and hair care products, as well (Atmanto, 2019) (Figure 1).

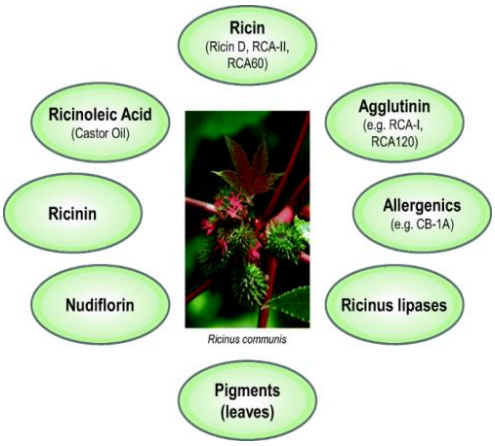

Figure 1. Major components of the plant *Ricinus communis* (cited after Franke et al., 2019)

From the economic point of view, the castor oil plant is valuable due to its beans' high oil yield. The chemical properties mainly reside in the molecular structure of the ricinoleic acid, turning the castor oil into a raw material important for the chemical and polymer industry, and an alternative in the production of biodiesel (Severino et al., 2012). The seed pomaces resulted from the oil extraction may be used in animal feeding (as a nourishing fodder), and as a pest repellent in agriculture (Chouhan, 2021).

2. The ricin – a vegetal protein with a toxic effect

Besides all the castor oil plant's therapeutic effects and economic value, the species is considered of risk and potentially harmful to the human health, due to its seeds' toxin. The chemical analysis of the seed endospermum detected a glycoprotein named ricin, a vegetal water-soluble toxin that has a cytotoxic effect on the human and on the animal living organisms (Severino et al., 2012). The ricin stops the type 2 ribosomes' activity. It is a heterodimeric protein containing two polypeptidic chains: the A chain (30 kDa), that induces the cytotoxic effects, and the B chain (32 kDa), proper to a lectin, a vegetal molecule with a high affinity for the membrane receptors in the eukaryotic cells. The B chain's role is the inner binding of the ricin in the process of endomitosis, the moment the A chain enters inside the cells, it exerts the toxic effects, by inhibiting the synthesis of proteins, which eventually leads to the cellular death. The process consists of a catalytic inactivation of the ribosome, removing a

specific adenine from the 4324 site in the 28 S rRNA, located in the 60 S ribosome subunit (Audi et al., 2005). The depurinated rRNA is subsequently unable to bind to the elongation factor 2 (eEF2), which inhibits the synthesis of proteins.
The ricin's high level of toxicity, its availability and easy manufacturing facilitated the use of this protein as a bioterrorism and warfare agent. The Center for Disease Control and Prevention (CDS) from the US has classified ricin as a category B threat agent, and as a Schedule 1 toxin by the Organisation for the Prohibition of the Chemical Weapons (OPCW) (Chen et al., 2014; Adibah et al., 2019).
Tons of ricin are produced each year worldwide, derived from the processing of the castor oil. This represents a menace to the human health. The ricin is absent in the refined oil, but is present in the seed pomace, resulted post- extraction.
No safe yet efficient cure in case of ricin intoxication was found so far (Sowa-Rogozinska et al., 2020). Research was focused on the development of innovative techniques to detect this toxin using a complex matrix, e.g.: castor bean flour, food, and human biological samples.

3. The ricin and its cytotoxicity mechanisms

Its toxicity resides in ricin's binding to the cell surface by its B chain, subsequently enters the cells by means of endocytosis (Bradberry et al., 2003; Sowa-Rogozinska, et al., 2020). The lysosome degradation, transport to the Golgi apparatus, followed by a reverse transport towards the endoplasmic reticulum. The ricin's A and B chains' cleavage takes place in the ER cisternal space (lumen). Inside the cytosol, the ricin's A chain inactivates the ribosomes by 28 S rRNA depurination inside the ribosomal subunit, a mechanism of inhibition of the protein synthesis, (Franke et al., 2019). This process stops the normal cell functions, causing the cellular death, ultimately.

4. The toxic effects induced by ricin

The scientific papers on this topic refer to over 1000 cases of ricin intoxication, caused by the ingestion of the castor seeds (Moshiri et al., 2016). The patients experienced the following symptoms: oropharingian irritation, abdominal pain, vomit, diarrhoea 4 to 6 hours post – ingestion, several types of gastrointestinal bleeding (hematemesis, melena, and hematochezia), dehydration.
The intoxication may occur by inhalation, injection, or accidental or intentional ingestion of the castor seeds or of the products that contain ricin (pomace or unrefined oil). The accidental intoxication comes from curiosity, self-medication, or confusion to other species' seeds. The voluntary intoxication reveals a suicide intent. The toxic effects depend on the ricin doses, that entered the organism, and with the type of exposure, as well. It is mandatory to emphasize that, in case of castor beans ingestion, the dosage vary both with their ricin amount, and with the number of ingested seeds. The references on this topic mention that a total number less than 30 ingested beans causes mild to severe, even lethal effects (Worbs, 2011).
The toxic doses of ricin were determined by means of the lab tests. The experiments on mice (*Mus musculus* L.) evinced that the average lethal dose (DL50) is of approximately 1000 times lower by injection or inhalation than by oral administration (ingestion). In humans, the inhalation exposure is more harmful than the ingestion (Balali-Mood et al., 2015). The calculated lethal dose for an adult is of about 3-5 μg per kilogram of body weight, in case of inhalation, whilst the DL50 for oral ingestion was estimated in between 1 to 20 mg of ricin per kilogram of body weight.
The toxicity of ricin has been tested in the lab and characterized (mainly the distribution and the excretion). It was evinced that the results depend on the tested experimental system, e.g.: the cell cultures' parameters, the *in vitro* tests, the animal species, the strains, the age and sex, the *in vivo* feeding conditions, as well as the injection/admission path and the duration of research (Franke et al., 2018). Therefore, it is extremely challenging to establish the precise lethal doses of ricin toxicity for humans.
The ricin is less toxic by ingestion due to the existing immune barriers within the intestins, to the characteristics of the stomach and of its epithelium (Audi et al., 2005). The ingestion of whole seeds evinced a low toxicity compared to the seeds crushed by mastication. The latter release a higher amount of toxin. The ingested ricin is absorbed, enters the blood and the lymphatic vessels, that spread the toxin in the entire organism. The toxin accumulates in liver (44%) and in spleen (33%). Its presence was evinced in the bone marrow (7.4%) and muscles (9%), as well. The trials on the animal species proved that, two hours after the ingestion, the ricin is detected in the faeces (Moshiri et al., 2016).
The dermic effect of the ricin is limited by its large molecules, that inhibits the absorption through the intact skin. Intraamuscular or subcutaneously injected, the ricin may be detected in urine in the next 24 hours (Moshiri et al., 2016). Though inhalation rarely occurs, the workers exposed to ricin powder experienced chest pain, eyelid rash, nasal and throat congestion, and hives (Ravinesh et al., 2022). By inhaling the ricin, the toxic effect ranges with the size of the particles deeply entering the lungs. In primates, it was evinced that inhaling 1 to 5 μm in diameter particles caused a higher toxicity compared to the inhalation of larger particles. The ricin's toxic effect after the inhalation determines the slow debut of an acute respiratory distress syndrome, cough, fever, lung lesions, pulmonary edema, palsy, and respiratory distress, causing death. No efficient antidote for this toxin is known until present. The other

vital organs may suffer, as well: the liver, the kidneys, and the small intestine appeared congested, and minor histological changes were evinced (Polito et al., 2019).
The effects of the ricin intoxication on the human body are varied, altering many systems and organs. One of the first noticed symptoms in intoxication is the presence of gastrointestinal disorders (nausea, vomit, diarrhoea, severe abdominal pain). They may be joined by dehydration and electrolite unbalance, by kidney failure, hepatic lesions, hematologic disorders, and respiratory distress (Worbs et al., 2011. The ricin is highly toxic, even in very low doses. Apart from the previously mentioned toxic effects, the ricin may cause tissular and cellular lesions in various body organs and tissues, altering the normal functions of the systems and of the organs. This causes longterm complications, and even a fatal outcome for the patients (Mijra et al., 2023).
The toxin eventually leads to the lisis in red blood cells. The patient's death occurs after 36 up to 72 hours in case of a lethal dose of ricin ingestion (Ravinesh et al., 2022). There follows a lag period of a few hours after the ingestion of ricin, displaying symptoms such as: vomit, diarrhoea, weakness, tachycardia, abdominal cramps, dehydration, dilated pupils (mydriasis), kidney malfunction, spinal cord palsy, and eventually death by the paralisy of the respiratory center.
In medical research, the ricin has been used within experiments to kill cancer cells. Therefore, research of ricin action in cancer patients displayed that the protein synthesis was inhibited. The toxin was administered by parenteral injection every other week in various doses ranging from 4.5 to 23 μg/mp. The potential of ricin as a chemotherapeutic agent was well received by patients (the dosage ranged from 18 to 20 μg/mp). The most obvious side effects were: fatigue, muscle pain, and nausea (Ravinesh et al., 2022).

5. The diagnosis in ricin intoxication

The toxicologic tests for the biological samples (blood, urine, faeces) in ricin intoxications are highly recommended to determine the severity of the process. A multitude of physico-chemical and immunological methods of analysis may be of use to detect and establish the level of ricin in an organism. The enzymatic activity is assessed using the enzymatic or the biochemical tests, implying a specific substrate, cleavaged by ricin. The enzymatic activity may be evinced by means of chemical or spectrophotometric reactions to evince the presence and the level of ricin in the analyzed samples. The immunological methods include the immune chromatography and the ELISA test, that use specific ricin-binding antibodies (Chen et al., 2014; Moshiri et al., 2016). The antigen – antibody reactions can be evinced by the color variation or by measuring the light absorption, offering data on the ricin level in the tested samples. The mass spectometry is an alternative method to detect ricin. It analyzes the molecular mass and the chemical structure through molecular ionization and fragmentation (Abbes et al., 2021).

CONCLUSION

Ricinus comunis L. is a well - known plant, due to its therapeutic properties. Both the vegetal extracts and the castor oil are used since ancient times as a remedy for various medical conditions.
The castor beans are a major oil source, containing mainly fatty acids, of which the ricinoleic acid is the most effective. The castor oil is a raw material for the chemical industry and the biodiesel manufacturing.
Along with the therapeutic effects and economic importance, castor oil plants have a harmful potential residing in the seeds' ricin – a glycoprotein that causes severe toxic effects in animals and in humans.
The ricin is a dangerous vegetal toxin, classified as a B category threat agent (can be used as a biological weapon). The toxicity of ricin comes from the protein synthesis inhibition in the eukaryotic cells. The most common symptoms of ricin poisoning are: vomit, nausea, abdominal cramps, diarrhoea, dehydration, respiratory distress.
Detecting the ricin poisoning is extremely important, regarding the fact that no antidote nor vaccine were yet found for its treatment.

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