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## Review Article

# Protective and Therapeutic Effect of *Physalis peruviana* L. in the Intoxicated Cases

<sup>1,2</sup>Said Said Elshama

<sup>1</sup>Department of Forensic Medicine and Clinical Toxicology, College of Medicine, Suez Canal University, Ismailia, Egypt

<sup>2</sup>College of Medicine, Taif University, Taif, Saudi Arabia

## Abstract

The treatment of some intoxication cases represents a challenge for the physicians, especially which are caused by some toxic agents that have not antidotes. Recently, major efforts are being done via using specific characteristic effects of some plants to treat these cases as a safe and effective alternative or adjuvant therapy. *Physalis peruviana* L. is considered as one of these plants. It possesses bioactive compounds such as phenolic compounds that can inhibit the lipid peroxidation activities inducing an antioxidant effect. This review aimed to assess the protective and therapeutic effect of *Physalis peruviana* L. in the treatment of some intoxicated cases. This review discovered that *Physalis peruviana* can modulate the toxic manifestations of cigarette smoke, cadmium, carbon tetrachloride and acetaminophen on the different body organs such as the lung, testes, liver and kidney. Moreover, the administration of this plant can also be beneficial in protection against carcinogenesis process in the lung and liver because of its antioxidant and anti-proliferative effects.

**Key words:** *Physalis peruviana*, antioxidants, carcinogenesis, bioactive compounds, anti-proliferative effects

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**Corresponding Author:** Said Said Elshama, Department of Forensic Medicine and Clinical Toxicology, College of Medicine, Suez Canal University, Ismailia, Egypt

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**Data Availability:** All relevant data are within the paper and its supporting information files.

## INTRODUCTION

Toxicological problems that affect human and animal health represent a challenge for the physicians especially with the common misuse of drugs and the widespread of environmental pollution. In the last years, many studies have focused on this challenge searching for an alternative therapy to treat some intoxication cases that are caused by some toxic agents that have not antidotes until now. Several studies utilized some specific characteristic effects of some plants in the treatment of some intoxication cases as a safe and effective alternative or adjuvant therapy. Therefore, these plants may be used as a promising source of modern curative and preventive agents in toxicity treatment<sup>1</sup>. The fruits of *Physalis peruviana* are one of these plants that were used in some studies as a poisoning treatment. It belongs to the family Solanaceae and called as Cape gooseberry or Harankash in Egypt<sup>2</sup>. In the past, its leaves and roots were utilized in folk medicine as a diuretic, antiseptic, antifungal, antibacterial, anticarcinogenic<sup>3</sup>, antimalarial and anti-inflammatory agent<sup>4</sup>. Phytochemical studies that were carried out on *Physalis peruviana* revealed that it has bioactive compounds such as physalins, glycosides, ticlopidine and phygrine that exert the beneficial health effects including the inhibition of xanthine oxidase and the lipid peroxidation activities<sup>5</sup>. It also contains minerals (iron, potassium, phosphorous and zinc), vitamins (A, B, C, E and K), carbohydrates, polyunsaturated fatty acids and fibers<sup>6</sup>.

The quantitative analysis of *Physalis peruviana* extract that was performed by using high-performance liquid chromatography (HPLC) showed that it contains phenolic compounds such as chlorogenic acid, rutin and caffeic acid that are responsible for many biological effects such as antioxidant effect. Recently, antioxidant properties of this useful plant are gaining attention of the scientists to use it in the medicine as an alternative therapy<sup>7</sup>. Moreover, Codevilla *et al.*<sup>8</sup> utilized the high-intensity ultrasound-assisted extraction (HIU) for the *Physalis peruviana* extraction wherein it showed similar results regarding phenolic and other antioxidant compounds besides demonstrating its cytotoxicity ability. Therefore, the current review focused on the role of *Physalis peruviana* L. as a preventive and therapeutic agent in the management of toxicity cases of drugs and other toxic agents according to the available researches.

## CIGARETTE SMOKE INTOXICATION

According to a lot of the published studies, the researchers discovered that *Physalis peruviana* has a potent

efficacy in modulating the toxic manifestations of a considerable number of toxic agents. It plays an important role in ameliorating intoxication of cigarette smoke<sup>9</sup>. Recently, many studies revealed that cigarette smoke contains harmful particles and trace amounts of microbial cell components such as bacterial lipopolysaccharide that plays a significant role in pulmonary diseases<sup>10</sup>. The cigarette smoke exposure usually changes the inflammatory mechanisms via enhancing the inflammatory cells influx including neutrophils in concomitant with the production of the inflammatory molecules leading to chronic obstructive pulmonary disease<sup>11</sup>. According to the results of many studies, the airway inflammation and neutrophil influx are major pathophysiological characters of chronic obstructive pulmonary disease wherein the persistent activation of neutrophils increases the reactive oxygen species production leading to the pulmonary tissue damage<sup>12</sup>. Moreover, macrophages produce inflammatory cytokines and chemokines that affect airway inflammation as one of the pathogenesis components of chronic obstructive pulmonary disease<sup>13</sup>.

Furthermore, cigarette smoke exposure causes high levels of tumor necrosis factor- $\alpha$  and interleukin-6 besides the production of monocyte chemoattractant protein-1 by macrophages and airway epithelial cells in the airway inflammatory response<sup>14</sup>. Therefore, antioxidants may have a therapeutic as well as a preventive role in cigarette smoke toxicity and then it can be beneficial in the treatment of chronic obstructive pulmonary disease via reducing the influx of inflammatory cells and the levels of inflammatory molecules and by upregulation of the antioxidant defense protein heme oxygenase-1. Thus, the antioxidants administration can ameliorate the airway inflammation with inhibition of monocyte chemoattractant protein-1<sup>15</sup>. In this context, Park *et al.*<sup>16</sup> used the antioxidant properties of *Physalis peruviana* to modulate the cigarette smoke toxicity and attenuate the airway inflammation via inhibition the neutrophil influx and the inflammatory toxic molecules such as reactive oxygen species that induce the pathogenesis of chronic obstructive pulmonary disease. Moreover, it also reduce the levels of pro-inflammatory cytokines such as tumor necrosis factor- $\alpha$  and interleukin-6 besides, it can attenuate the expression of monocyte chemoattractant protein-1 in concomitant with an increase in the nuclear factor erythroid 2-related factor 2 activation and heme oxygenase-1 (HO-1) expression. Therefore, this plant is considered as a valuable therapeutic adjuvant in cigarette smoke-induced airway inflammatory diseases such as chronic obstructive pulmonary disease.

Cigarette smoke is considered as the most common cause of the lung cancer wherein the tobacco smoke contains two main carcinogenic components that are polycyclic aromatic hydrocarbons and nitrosamines. Nitrosamine 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone that is called as nicotine-derived nitrosamine ketone (NNK) is considered as the key ingredient of the tobacco smoke carcinogen which plays a vital role in the carcinogenesis of the lung<sup>17</sup>. El-Kenawy *et al.*<sup>18</sup> evaluated the efficacy of *Physalis peruviana* on the toxic effect of NNK induced lung cancer by using the pulmonary histopathological, immunohistochemical and DNA flow cytometric analysis. They proved that the administration of *Physalis peruviana* could protect against NNK induced-lung carcinogenesis because of its antioxidant and anti-proliferative effects<sup>18</sup>.

### ACETAMINOPHEN INTOXICATION

In another context, Chang *et al.*<sup>19</sup> concluded that *Physalis peruviana* has a hepatoprotective effect against acetaminophen-induced hepatotoxicity based on its ability to induce the cell membrane stabilization, hepatic cell regeneration and enhancing the activity of antioxidants enzymes such as catalase, superoxide dismutase and glutathione peroxidase. Furthermore, it can normalize the levels of hepatic enzymes associated with a prominent amelioration in the toxic manifestations of hepatic injury such as cell necrosis and fatty changes in a dose-dependent manner.

Moreover, Hassan *et al.*<sup>20</sup> conducted another study to assess the free radical scavenging activity and the antioxidant capacity of *Physalis peruviana* which indicated its ability to antagonize the free radicals generation and activate the antioxidant defense mechanisms leading to a marked improvement in the levels oxidant and antioxidants parameters besides the levels of hepatic biomarkers. Hassan *et al.*<sup>20</sup> also reported that this plant could increase significantly the antioxidant biomarkers levels including total antioxidant capacity, catalase and superoxide dismutase associated with a decrease in the malondialdehyde level.

### CARBON TETRACHLORIDE INTOXICATION

In another context, Abdel Moneim<sup>21</sup> used *Physalis peruviana* to prevent the testicular toxicity that was caused by carbon tetrachloride. This study indicated that *Physalis peruviana* juice supplementation could improve the

sex hormones levels such as testosterone, luteinizing hormone and follicle-stimulating hormone besides the activation of the testicular antioxidant enzymes such as glutathione peroxidase, glutathione-S-transferase, catalase, superoxide dismutase and glutathione reductase that are suppressed by the administration of carbon tetrachloride. In addition, it can also decrease the lipid peroxidation and the nitric oxide production in concomitant with prevention of the germ and Leydig cells degeneration, spermatogenesis deformities and the caspase-3 activity inhibition attenuating the apoptosis in the testicular tissues. Therefore, *Physalis peruviana* may have a therapeutic and preventive role in the free radical-mediated diseases, the reproductive toxicity and infertility<sup>21</sup>.

### CADMIUM INTOXICATION

Abdel Moneim *et al.*<sup>22</sup> carried out another study to investigate the effect of *Physalis peruviana* on cadmium-induced oxidative neurotoxicity in the brain. This plant successfully corrected the disturbance of the neurochemical parameters wherein it restored the normal levels of dopamine, serotonin and 5-hydroxyindoleacetic acid in hippocampus cerebellum and cerebral cortex in association with a decrease in the levels of nitric oxide and lipid peroxidation in the brain. It also increased the activity of non-enzymatic and enzymatic antioxidants significantly along with restoring the normal glutathione<sup>22</sup>. In the related context, Othman *et al.*<sup>23</sup> proved the efficacy of *Physalis peruviana* in ameliorating another toxic manifestation of cadmium that is the testicular toxicity. It decreased the testicular levels of malondialdehyde, nitric oxide and caspase-3 expression along with an increase in the glutathione content and the activities of catalase, superoxide dismutase, glutathione peroxidase, glutathione reductase and the testosterone level. Moreover, the testicular oxidative stress and the germ cell apoptosis besides the testicular histopathological changes were improved via the protective effect of *Physalis peruviana*<sup>23</sup>.

In addition, Dkhil *et al.*<sup>24</sup> concluded that this precious plant has also a protective role against cadmium-induced hepatotoxicity and nephrotoxicity. It reduced the lipid peroxidation, nitric oxide and increased the activities of the enzymatic and non-enzymatic antioxidant molecules and glutathione in the tissues of liver and kidney, reversing the toxic histopathological changes. Moreover, *Physalis peruviana* increased the expression of Bcl-2 protein in liver and kidney besides its antioxidant and anti-apoptotic effects.

## CONCLUSION AND RECOMMENDATION

The protective and therapeutic efficacy of *Physalis peruviana* L. was proved significantly in the treatment of toxic manifestations of some toxic agents such as cigarette smoke, cadmium, carbon tetrachloride and acetaminophen. The administration of *Physalis peruviana* L. can also protect against carcinogenesis process in the lung and liver because of its antioxidant and anti-proliferative effects. In the future, further studies should be conducted in vitro to assess the role of *Physalis peruviana* L. in the treatment of other types of intoxication along with other studies *in vivo* to prove its preventive and therapeutic role in the treatment of toxicity.

## SIGNIFICANCE STATEMENT

Finally, this study discovered the efficacy of *Physalis peruviana* L. as an alternative and complementary therapy in treatment the toxic manifestations of cigarette smoke, cadmium, carbon tetrachloride and acetaminophen that can be beneficial for physicians and clinical toxicologists. This study will also help the researchers to uncover the critical areas in the treatment of some toxic agents that many researchers were not able to explore its antidotes until now. Thus, a new theory on using alternative therapy in the treatment of this type of intoxication cases may be arrived at.

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