



# Effect of Some natural products against Ehrlich Ascites Carcinoma in mice: A Review

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## Abstract

Cancer is a serious disease and it is one of the main causes of death, and it is considered the second cause, after people who suffer from heart failure. Through the statistics, Breast cancer is one of the most common types of cancer, with a rate of 99% in women and 1% in men. It is very complex, and patients with this type of cancer may face numerous challenges during their treatment period. It was determined that the death rate from cancer had decreased by 1.5%, but it is expected to increase in the future due to an increase in cancer cases (breast, prostate). Ehrlich model is a cancer that grows inside a mouse. Its origin is spontaneous mammary carcinoma, and when it spreads within the mouse, it takes two forms, either ascitic or solid. Ehrlich's ascites carcinoma is a spontaneous breast cancer that has a very high importance in scientific research. It is undifferentiated and has a short life. This type of cancer was used for the first time in 1932, when it was used inside the mouse in the abdomen, and a type of fluid was obtained for this called ( Ehrlich's ascites) due to the liquid substance on which cancer cells depend and consider it food and a means for rapid tumor growth, EAC deficiency causes anemia and thus causes a decrease in red blood cells or hemoglobin, EAC causes an increase in urea and a decrease in creatinine, and EAC causes an increase in liver enzymes and a decrease in total protein. Natural products are the only and most effective products that lead to the development of drugs, especially anti-cancer drugs and anti-inflammatories. Through studies, it has become clear that natural products are a source of drugs.

**Keywords:** natural products, Ehrlich ascites carcinoma, DNA damage, Ehrlich model.

## 1. Introduction

Scientists have tried to do everything they can to prevent the spread or development of cancer (Perveen et al., 2012). Cancer is a disease caused by more than one cause, such as chemical, genetic, and nutritional metabolism (Hassan et al., 2019). For cancer, treatment by radiation or chemotherapy are traditional treatments, but. Cancer is one of the causes that lead to death (Hegazi et al.,

2011). One of the factors that reduce the effectiveness of cancer, which has been used in recent years, is the interest in fruits and vegetables (Hassan et al., 2010). Through statistics, it became clear that the death rate due to cancer decreased by (1.5%), but it is expected that it may increase in the future due to the increase in the incidence of cancers (breast, prostate). In 2023, about 1,958,310 cases were recorded for those infected. According to the National Center for Health Statistics in the United States, the incidence of

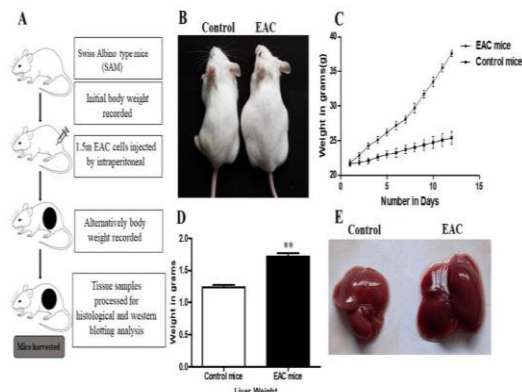
prostate cancer has increased, the incidence of lung cancer has decreased in women, and the incidence of breast cancer in women has continued to rise, as well as cancers (liver and skin) (Siegel et al., 2023). Breast cancer is the most prevalent type in women and its spread leads to death, and when diagnosing more than 90% of the patients, it turns out that it is of the early type, and approximately 30% of the early type will have a recurrence (Nelson et al., 2022).

In 2015, 2.4 million breast cancer patients were tested 523,000 died. When breast cancer is detected early, the ability to treat is more when it is discovered late, through certain screening programs. One of the requirements for breast cancer screening is the presence of one or two radiologists. This is for screening mammograms to diagnose breast cancer early and reduce deaths from breast cancer (Freeman et al., 2021). In high-income countries, the death rate from breast cancer is decreasing due to improved treatments and the result of continuous x-ray examination, and because of the burden of disease on women, this type of cancer will affect one in every eight women over the age of 85 (Britt et al., 2020). One of the risk factors for breast cancer is low physical activity, and it can play an important role in surviving the infection, according to some reports of experts of the 2018 Continuous Update Project issued by the World Cancer Research Fund (WCRF), and that recommendations for physical activity for breast cancer survivors are based on extrapolation from Cancer prevention recommendations, because the evidence that physical activity reduces the death rate from breast cancer is still insufficient (Samoli et al., 2019). Breast

cancer is of a complex nature, and the treatment period can go through many difficulties. Modern technologies contributed to the early detection of breast cancer by analyzing the number of plasma CTC or detecting ctDNA for the purpose of primary detection of breast cancer and helping doctors predict the diagnosis of the disease and start the treatment process (Alimirzaie et al., 2019). The early examination of breast cancer has positive effects on the survival of patients over the past 30 years, and the promotion of treatment for the early stages of the affected person. As a result, a group of people with metastatic breast cancer (mBC) can be treated through combination therapy. The resistance of a person with breast cancer to treatment is the biggest challenge, so the majority of mBC cases are not cured and lead to the death of about 500,000 people each year (Pasha et al., 2021).

Three main types of breast cancer depend on the presence of hormone receptors (estrogen, progesterone, and human epidermal growth factor 2 ERBB2), most cancers do not grow inside the body at diagnosis (Waks et al., 2019). Triple-negative cancer is considered one of the types of breast cancer that does not express receptors like other types, but it has its own characteristics such as the ability to relapse and poor prognosis, so far the stages of treatment of triple-negative cancer are missing, so the development of treatments for this type of cancer has become a necessary need (Dumas et al., 2020). Ehrlich ascites carcinoma (EAC) is induced in the mouse by intraperitoneal injection of tumor cells (Hassan et al., 2019). After transplanting Ehrlich's ascites cells, it was found that there was an increase in the weight of the mice that carried Ehrlich ascites, compared to the mice that did not carry Ehrlich's ascites, which are the control mice (Figure-1. Ehrlich's ascites and control mice Figure-1) (Gowda et al., 2022). Ehrlich model

is a cancer that is grown inside the mouse. Its origin is spontaneous breast cancer, and when it spreads inside the mouse, it takes two forms, either ascitic or solid form (Abd Elrazik et al., 2022).



**Figure.1: Difference between Normal Hepatic and EAC-Bearing Liver (Gowda et al., 2022).**

## 2.2. Ehrlich Ascites Carcinoma

Ehrlich's ascites carcinoma (EAC) is of great importance in laboratory experiments, and it is considered undifferentiated, has a high ability to transplant, has a short life, 100% malignant cells, grows rapidly in vivo, many experiments have been conducted on carcinoma Ehrlich's ascites in the past decades, and scientists have concluded that some of the plant extracts had the ability against EAC. Ehrlich's ascites (EAC) and breast cancer are used inside a female mouse in the abdomen. In 1932, this was done. A type and a liquid form was obtained in the mouse and for this reason it was called Ehrlich's hydrocephalus "because of the fluid of the cancer cells, and work also continued in 1972 on Ehrlich's ascites carcinoma EAC (Ozaslan al., 2011). Cancer cells inside mice depend on ascitic fluid and consider it a food source for them and it is considered an essential means for tumor growth. Through studies, it has been shown that Ehrlich's ascites carcinoma

(EAC) affects anemia and thus leads to a decrease in red blood cells or hemoglobin (Abd Elrazik et al., 2022). Ehrlich's ascites carcinoma (EAC) causes anemia due to iron deficiency, and an increase in the number of white blood cells occurs in mice bearing Ehrlich's ascites carcinoma (EAC) compared with control mice (Dashora et al., 2011). EAC is frequently used in vivo to investigate its effect in vivo. It was observed that EAC causes an increase in MDA lipid peroxidation in EAC-bearing mice, and that GSH and Catalase cat enzymes are decreased in EAC-bearing mice compared to control mice (Sannigrahi et al., 2012). Ehrlich's ascites carcinoma (EAC) caused an increase in the percentage of neutrophils compared to the control group, while it caused a decline in lymphocytes and monocytes when compared to the control group (Singh et al., 2011).

EAC causes a rise in plasma lipid peroxidation levels (TBARS) when compared to control mice (Adriana et al., 2006). Studies have shown that EAC-bearing mice show lower levels of interferon and interleukin-2 compared to control mice (Sheeja et al., 2007). Scientific research has shown that EAC causes an increase in glutathione peroxidase (Gpx) in EAC-bearing mice, as well as an increase in hydrogen peroxide ( $H_2O_2$ ) and myeloperoxidase (MPO) compared to control mice (El Sayed et al., 2020). Induction of EAC cells at a dose of  $1 \times 10^6$  cells/ml in vivo results in lower liver total protein, higher total cholesterol and triglycerides in EAC-bearing mice compared to control mice, and a decrease in superoxide dismutase (SOD) and GSH-glutathione in EAC-bearing mice compared to control. with control mice (Mallapur et al., 2021). EAC cells cause an increase in Tumor Necrosis Factor Alpha (TNF- $\alpha$ ) and Total Antioxidant Capacity (TAC) of EAC-bearing mice when compared to control mice (Awad et al., 2019). EAC cells cause an increase in

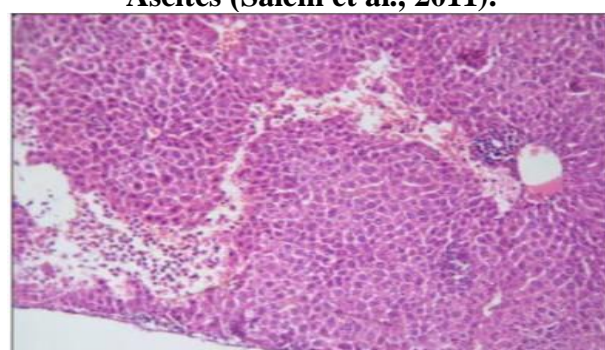
plasma urea, a decrease in plasma creatinine, and damage to EAC-bearing liver tissue compared to control mice (Mansour et al., 2020).

Induction of EAC cells at a dose of  $2 \times 10^6$  cells per mouse intraperitoneally and after 10 days, the effect of liver enzymes (Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST) and Alkaline Phosphatase (ALP)) increased in carrier mice. EAC cells compared to control mice, total protein is decreased in EAC cell carrier mice, and bilirubin is increased in EAC cell carrier mice compared to control mice (Munira et al., 2013). Induction of EAC cells at a dose of  $2 \times 10^6$  cells per mouse intraperitoneally and after 10 days, affected leukocytes and neutrophils increased, lymphocytes and monocytes decreased in EAC-bearing mice as compared to control mice, and erythrocytes and hemoglobin were decreased in EAC-bearing mice in comparison with control mice (Kandar et al., 2012). Ascitic fluid provides appropriate food for cancer cells, which helps them to spread in vivo, and we note an increase in the tumor size of EAC-bearing mice (Islam et al., 2008). Induction of EAC cells at a dose of  $2 \times 10^6$  cells per mouse into the peritoneum and after 10 days, leads to swelling in the mouse, which indicates an increase in weight and tumor spread Figure-2, and causes damage to the liver tissue of EAC-bearing cells Figure-3. (Salem et al., 2011). Induction of EAC cells at a dose of  $2 \times 10^6$  cells per mouse into the peritoneum and after 14 days, damages the murine kidney DNA of EAC-bearing cells Figure-4, and causes kidney tissue damage to EAC-bearing cells Figure-5. DNA damage plays an important role in

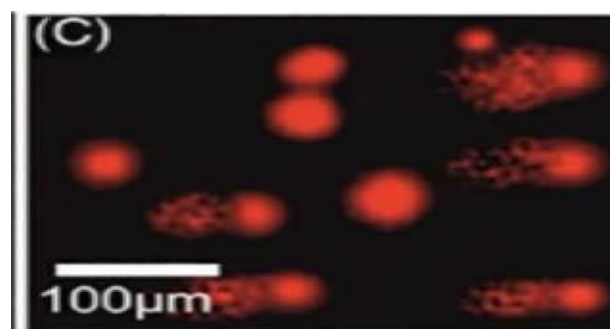
the pathophysiology of people with cancer, and there is much evidence proving the spread of damage in people with the disease (Wang et al., 2023).



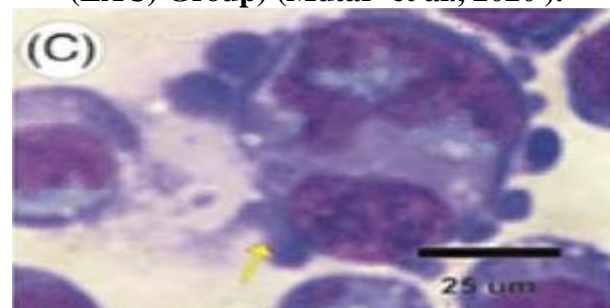
**Figure. 2: Ehrlich-Bearing Mice Showing Ascites (Salem et al., 2011).**



**Figure.3: The Effect of EAC Tumor Cells on the Hepatic Tissue (Salem et al., 2011).**



**Figure.4: Effect of DNA Damage in Renal Tissue of Mice Bearing EAC Cells. (C, (EAC) Group) (Mutar et al., 2020).**



**Figure.5: A swab of ascitic fluid for EAC cells, C) Showing Fewer Cancer Cells, Expansion of the Nucleus (Mutar et al., 2020).**



### 3. Role of some natural products against EAC

Natural products are the only and most effective products that lead to the development of medicines, especially anti-cancer and anti-inflammatory drugs, and work has been done to develop examinations for ease of use of natural products and thus develop the process of drug detection (Harvey et al., 2008). Through study, it became clear that natural products are a source of medicines, and also natural products are considered active against many infectious diseases because most of these products were developed from microbial warfare (Rouhi et al., 2003). Studies in recent years on natural products have had a high momentum due to their effectiveness against chronic diseases, and these products, known for their unique chemical diversity and vital activity, continued to provide many templates for drug development, and modern techniques for isolation of natural extracts, detection of the natural product and active substance, and quality control were developed. These products include GC-MS, LC-PDA, LC-MS, LC-FTIR, LC-NMR, LC-NMR-MS and CE-MS (Hasan et al., 2023). The work of natural products continued for centuries as a major source of medicines, and half of the pharmaceutical preparations at the present time were prepared from natural products, and one of the reasons for the interest in natural products in recent years (Clark et al., 1996). Natural products have had a wonderful work for more than 40 years against cancer. The microbes from which natural products were prepared act as an essential source against cancer. Because of the high toxicity of some drugs for cancer chemotherapy and the rapid resistance to these drugs, research is continuing on new natural products that have effectiveness against

cancer (Demain et al., 2011). Cancer is the second cause of death in this era, and there has become a necessary need to use natural products as a prevention against cancer without these natural products causing side effects on human health, such as vegetables, herbs, and plant extracts (Reddy et al., 2003). Through natural product studies, methanol extract of *Caesalpinia bonducella* (MECB) extract was evaluated in EAC carcinoma-bearing Mice, at different doses of 50, 100, and 200 mg/kg. By affecting levels close to normal for each of the hepatic lipid peroxidation and the free radical scavenging enzyme GSH, CAT and SOD, and the extract had no side effects (Gupta et al., 2004). Studies have shown that ethanol extract of *Pisonia aculeata* (EEPA) It has an effect on EAC cancer, the extract EEPA was given to EAC-bearing mice in two different doses (250 and 500 mg / kg / day), and after the end of the treatment period, it was proven that the extract EEPA reduces the size of the tumor produced by EAC cells (Senthilkumar et al., 2008).

Show extract treatment methanol extract of *Bauhinia racemosa* (MEBR) On EAC-bearing mice, different doses (50, 100, 200, and 400 mg/kg) had a protective effect on tumor proliferation, hemoglobin, and erythrocytes as compared to control mice (Gupta et al., 2004). That treatment cranberry extract at two different doses (75 and 150 mg/kg body weight) for 21 days in EAC-bearing rats, it had a significant effect on glucose, insulin, alanine transaminase (ALT), aspartate transaminase (AST), and alkaline phosphatase (ALP). , lactate dehydrogenase (LDH), total cholesterol (TC), triglyceride (TG) as compared to EAC-bearing mice (Hussien et al., 2015). prevention *Commiphora molmol* (oleo gum resin ) EAC-bearing mice with different doses (125-500 mg/kg) It has a significant effect on the salts in the body such as (Na, k and Ca) (Qureshi et al., 1993). Show that prevention *Costus Speciosus* At a dose of (5 g / kg) it has a significant effect on EAC cancer cells in female mice, EAC caused an increase in the levels of CEA, CA19-9 and the

level of cholesterol in the blood, and when prevention was *Costus Speciosus* observed a decrease in the levels of CEA and CA19-9 and the level of cholesterol in the blood compared to mice EAC-bearing (Abdel-Maksoud et al.,2014).

Studies showed that treatment with flaxseed oil and corn oil showed a significant improvement in EAC-bearing rats, where the results showed that both (liver enzymes and alpha-fetoprotein) were improved in the treatment groups with flaxseed oil and corn oil compared to the group that carried EAC. EAC, and the treatment also showed an improvement in the hepatocytes, as the hepatocytes appeared normal compared to the EAC-bearing cells (El-khayat et al., 2016). Treatment with purslane seed oil at a dose of (200 gm/kg diet) and 5-fluorouracil at a dose of (20 mg/kg body weight) against EAC-bearing rats showed positive effects on 17 $\beta$ -estradiol and progesterone, and the combination of the two treatments produced a very high effect on 17 $\beta$ -estradiol and progesterone against EAC tumor-bearing mice (Ali et al.,2014).

It was shown *Lactuca serriola* to have high efficacy against EAC, as hematological parameters such as hemoglobin, red and white blood cells were improved compared to EAC-bearing mice (Alshathly et al., 2014 ). The prevention B-Glucans extract (BG) shows good results on EAC cells, as it affects kidney functions such as urea and creatinine compared to EAC-bearing mice, and also improves renal cells, as we notice mild atrophy in the kidney tissues of mice that were treated with tB-Glucans extract (BG) ( Hasan et al.,2023).

## Conclusion

Natural products are widely used in scientific research because of their high efficacy and showed activity against

Ehrlich's ascites carcinoma (EAC) in mice.

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### تأثير بعض المنتجات الطبيعية ضد سرطان الاستسقاء ايرليش في الفئران: مراجعة

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### الخلاصة

السرطان مرض خطير وهو أحد الأسباب الرئيسية للوفاة، ويعتبر السبب الثاني بعد الأشخاص الذين يعانون من قصور القلب. ومن خلال الإحصائيات، يعتبر سرطان الثدي من أكثر أنواع السرطان شيوعاً، حيث تصل نسبة الإصابة به إلى ٩٩% لدى النساء و ١% لدى الرجال. إنه أمر معقد للغاية، وقد يواجه المرضى المصابون بهذا النوع من السرطان تحديات عديدة خلال فترة علاجهم. وتبين أن نسبة الوفيات بسبب السرطان قد انخفضت بنسبة ١,٥%، ولكن من المتوقع أن ترتفع مستقبلاً بسبب زيادة حالات السرطان (الثدي، البروستاتا). نموذج إيرليك هو سرطان ينمو داخل الفأر. أصله هو سرطان الثدي العفوي، وعندما ينتشر داخل الفأرة يأخذ شكلين، إما استسقاء أو صلباً. سرطان استسقاء إيرليك هو سرطان ثدي عفوي له أهمية كبيرة جداً في البحث العلمي. إنه غير متميز وله عمر قصير. تم استخدام هذا النوع من السرطان لأول مرة عام ١٩٣٢، حيث تم استخدامه داخل الفأرة في البطن، وتم الحصول على نوع من السوائل لهذا يسمى (استسقاء إيرليك) بسبب المادة السائلة التي تعتمد عليها الخلايا السرطانية وتعتبرها إنه غذاء ووسيلة لنمو الورم السريع، نقص EAC يسبب فقر الدم وبالتالي يسبب انخفاض في خلايا الدم الحمراء أو الهيموجلوبين، يسبب EAC زيادة في اليوريا وانخفاض في الكرياتينين، و EAC يسبب زيادة في إنزيمات الكبد وانخفاض في الكرياتينين. البروتين الكلي. المنتجات الطبيعية هي المنتجات الوحيدة والأكثر فعالية التي تؤدي إلى تطوير الأدوية، وخاصة الأدوية المضادة للسرطان ومضادات الالتهابات. ومن خلال الدراسات تبين أن المنتجات الطبيعية هي مصدر للأدوية.