



# Effect of 1-((2-hydroxyphenyl)iminomethyl)naphthalene-2-ol on a Biochemical and Hematological Markers in Ehrlich Ascites Carcinoma Bearing Mice

Rasha Fekry Zahran<sup>\*1</sup>, Rahma M. Elsaka<sup>1</sup> and Mostafa A. Diab<sup>2</sup>

<sup>1</sup>Biochemistry division, Chemistry Department, Faculty of Science, Damietta University, 34517 Damietta, New-Damietta, Egypt.

<sup>2</sup>Chemistry Department, Faculty of Science, Damietta University, Damietta, Egypt.

Received: 10 September 2024 /Accepted: 12 September 2024

\*Corresponding author's E-mail: rzahran17@yahoo.com

#### Abstract

Background: Some Currently, several Schiff base compounds are among the most essential building blocks for the creation of novel medications. The purpose of this assayment is the study of the anti-oxidant and anti-tumor effects of [1-((2-hydroxyphenyl) iminomethyl)naphthalene-2-ol] that is directed against the Ehrlich ascites carcinoma (EAC) cells seen in the male albino mice's peritoneal cavity.

Methods: Six groups of adult male Swiss albino mice were created: group I served as a negative control and received salt saline; group II received DMSO; group III received the tested substance; group IV, the EAC-bearing group served as the positive control.; mice were injected intraperitoneally (I.P.) with EAC cells (2.5x106 cells/m on day 1; group V served as a therapeutic group; mice were injected intraperitoneally (I.P) with therapy (0.05 mg/kg for a duration of 14 days). Study efforts were conducted about some biochemical parameters.

Results: Our results showed a significant increase in biochemical parameters concerning the negative control group. Therapy with [1-((2-hydroxyphenyl) iminomethyl)naphthalene-2-ol] appeared to be effective against EAC and biomarker changes induced by EAC, as evidenced by the improvement of the same parameters.

Conclusion: [1-((2-hydroxyphenyl) iminomethyl) naphthalene-2-ol] has good antioxidant and antitumor properties.

Keywords: Ehrlich ascites carcinoma; anti-oxidants; antitumor; Schiff bases.

#### Introduction

Cancer is a hereditary illness caused by Deoxy

nucleic acid (DNA) mutations that alter the homeostasis of tissues and/or cell survival and/or death (Hrubisko et al., 2010). Cancer cells can spread to locations distant from where they originated (Dayem et al., 2010). The most prevalent health issue and cancer is the primary cause of mortality globally. (Agrawal et al., 2011).

A number of chronic diseases can be delayed or prevented by antioxidants, which are chemicals that lessen the passive effects of free radicals on the body's metabolism (Willcox et al.. 2004) The hunt for innovative pharmaceuticals with antioxidant properties has grown in recent years in medication design studies, thus it is believed that multifunctional medications with antioxidant activities can help remove undesirable drug side effects and free radicals created by metabolic processes (Tuo et al., 2022)

A mouse mammary adenocarcinoma called Ehrlich ascites carcinoma (EAC) develops on its own that grows quickly, lacks differentiation, and is completely cancerous. Because cancer cells spread throughout patients' internal organs as ascites forms in the peritoneum, the characteristics of EAC are similar to those of human cancers (Abd Eldaim et al., 2021). Ehrlich tumors are a transplantable tumor model that have been utilized to conveniently examine the anticancer properties of several chemical substances (Tousson et al., 2020).

Under some circumstances, imines, which are Schiff bases, are typically the condensation products of primary amines with carbonyl compounds. (Omer et al., 2021). The azomethine (-CH = N-) functional group that characterizes Schiff base derivatives was initially identified by Hugo Schiff (Kumar and Roy 2022). These substances have been found to have several biological effects, including as antitumor (Bashiri et al., 2021) and antioxidant (Saleem et al., 2021).

Applications for Schiff base complexes in biological and analytical disciplines are numerous (Okamoto, 2023). Particularly in the pharmaceutical and medical industries, schiff bases were an important class of chemical molecules. Therefore, the development of new Schiff base derivatives and their prospective use as chemotherapeutics has kept organic and medicinal chemists interested (El-Sonbati et al., 2022).

More potent than phenols, naphthols are phenol's naphthalene homologs. Nature contains a number of naphthol derivatives that are being studied for their pharmacological and biological properties. One useful core structure for the production of several medications is 1naphthol ( $\alpha$ -naphthol) (Brągoszewska et al., 2020). Dyes used in foods (e.g., azorubine, martius yellow), bioactive molecules, and vitamins (e.g., K5 and K7). Substituted 1naphthols have a broad spectrum of biological activities, such as anticancer (Hsu et al., 2017), anti-inflammatory (García et al., 2018), antiviral (Ho et al., 1996), antimalarial (Wang et al., 2020) and antibacterial (Sun et al., 2011) properties. 1-Naphthol is a metabolite of the insecticide carbaryl (1-naphthyl methylcarbamate, Sevin) and naphthalene (Meeker et al. 2006).

The purposes of the current research are to study the anti-tumor effect of [1-((2hydroxyphenyl)iminomethyl)naphthalene-2-ol] against EAC cells, evaluate how well the substance destroys cancerous cells, and evaluate its impact on biochemical indicators.

# Materials and Methods

# Animals

Adult male Swiss albino mice weighed 20 to 25 g were purchased from Cairo, Egypt's Al Azhar University's Regional Center for Mycology and Biotechnology. Before the experiment began, the mice underwent a 7-day acclimatization period in steel mesh cages (Animal House, Faculty of Science) while being fed a pellet meal and given access to unlimited amounts of water.

# Transplantation of EAC cells

Ehrlich ascites carcinoma cells were isolated and suspended in sterile 4-isotonic saline from donor mice obtained from Cairo University's Egyptian National Cancer Institute. A healthy mouse received an intraperitoneal transplant of  $2.5 \times 10^6$  cells/ml.

# Chemistry

# [1-((2-

hydroxyphenyl)iminomethyl)naphthalene-2-ol] Figure 1 was created using the procedure outlined(El-Sonbati, Diab, Morgan, et al. 2022). The compound was dissolved in (1% DMSO) to give solution.

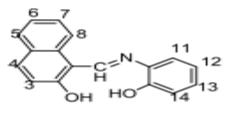


Figure 1: The chemical structure of [1-((2-hydroxyphenyl)iminomethyl) naphthalene-2-ol].

# *Revelation of the therapeutic compound's median lethal dosage (LD50)*

Meier and Theakston's technique revealed the median lethal dose (LD50) of the studied chemical (More et al., 2022). The recommended limit dose cannot be determined without further research to ascertain the LD50. To determine the compound's LD50, 40 mice (four for each dose) were given injections of 1, 1.5, 2, 2.5, 3, 3.5, 4, 6, 8, and 10 mg/kg of the compound's sodium salt, respectively. The mice were then observed for a whole day. 16 additional mice (4 mice for each dose) received injections of 50, 100, 150, and 200 mg/kg, respectively, and were allowed to perceive the effects for 24 hours.

## Experimental design

Five sets of twenty male Swiss albino mice each, weighing between twenty and twenty-five grams, were created as follows: Group 1 (G1): negative control group: for a period of 14 days, mice received intraperitoneal injections of sterile saline solution (0.9% NaCl). Group 2 (G2): DMSO group: for 14 days, mice received intraperitoneal injections (I.P) of (1% DMSO).

Group 3 (G3): drug group; for 14 days, mice received intraperitoneal injections (I.P) of a synthetic substance at a dose of 0.05 mg/kg.

Group 4 (G4): Positive control (EAC-bearing group) mice received a single intraperitoneal injection I.P on day 1 of  $2.5 \times 10^6$  EAC cells/mice.

Group 5 (G5): therapeutic group; The day following the injection of EAC, mice received intraperitoneal injections (I.P) of a synthetic substance at a dose of 0.05 mg/kg for a duration of 14 days.

#### Collection of blood samples

When the experiment came to an end, mice were put to death with CO2. The

peritoneal cavity was carefully opened. Blood samples were drawn from `the inferior vena cava and divided into two halves. In an EDTA glass tube, one half was used as an anticoagulant to get the complete blood count. The remaining half was contained in heparinized glass tubes and was utilized to estimate biochemical indicators.

## Collection of tissue sample

Each mouse's hepatic tissues were removed, washed in cold saline, and split into pieces. The piece of the hepatic tissues was removed and preserved in phosphates buffer saline (PBS) (PH 7.4) for tissue homogenate readiness.

#### Studies of in vitro cytotoxicity

## Assay of MTT

A modified version of the standard 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2Htetrazolium bromide(MTT) assay was used to measure in vitro cytotoxicity for each test system (Doudach et al. 2022). In summary, Roswell Park Memorial Institute (RPMI) medium suspended with 10% FBS was used to raise the number of EAC cells extracted from the peritoneum of mice given an EAC injection to  $1 \times 10^5$  cells/ml. A 96-well plate containing 100 µl of EAC cells was cultured for 48 hours at 37°C in a CO<sub>2</sub> incubator with varying dosages of 6-FU and the tested drug. Cell cultures were treated with 100 µl MTT reagent (1 mg/ml) for 4 hours at 37°C after the medium was removed after 48 hours. One hundred microliters of DMSO were added to solubilize the formazan that the live cells produced. After five minutes of incubation in a shaker, the 96well plate containing the cell suspension was measured for absorbance at 570 nm using a reader. The percentage microplate of cytotoxicity and IC50 values were then computed.

#### Measurements

# Hematological examination

(Sysmex kx-21n automated hematology analyzer, made by JAPAN CARE CO., LTD.,) was used to automatically analyze the complete blood count (CBC).

#### Biochemical markers

#### Detection of hepatic and renal function tests

Using a commercial kit provided by Spinreact (Santa Coloma, Spain), the activities of serum glutamic pyruvic transaminase (SGPT) and serum glutamic oxalo acetic transaminase(SGOT) in plasma were detected using the Reitman and Frankel method (Ngumah et al. 2023). A commercial kit (GENISIS, Egypt) was used to quantify the plasma creatinine levels in accordance with (Hameed et al., 2022).

# Measurement of oxidative stress markers in liver homogenate

The method outlined was used to measure the level of total antioxidant capacity (TAC) in hepatic tissue (Bindhu et al., 2023) using the Biodiagnostic kit (Biodiagnostic Company). We evaluated malondialdehyde (MDA) using Satoh's method (Tassa et al., 2023) by a Biodiagnostic kit (Biodiagnostic Company, Egypt).

#### Statistical analysis

Utilizing the Statistical Package for Social Sciences version 20 (SPSS), statistical analysis was conducted, and the findings were displayed as mean  $\pm$  SD. The ANOVA test was used to compare the average values of the variables under study between the various groups. P-values <0.05 and <0.01 were regarded as significant and very significant, respectively (El-Ansary et al., 2021).

## Results

#### Median lethal dose (LD50) of the compound

By administering the tested substance intraperitoneally, the acute toxicity was evaluated, and the median lethal dose of the substance was determined. The findings showed that the substance was safe up to 0.05 mg/kg, at which point no death rate was noted.

## In vitro cytotoxic study

#### [1-((2-hydroxyphenyl)iminomethyl)

naphthalene-2-ol] has shown concentration dependant cytotoxicity on EAC cells in MTT assay, the IC50 values of  $[1-((2-hydroxyphenyl))minomethyl)naphthalene-2-ol] was 625 \mu M /ml in MTT assay.$ 

#### Biochemical analysis

#### Changes in hematological parameters

Table 1 stated the effects of the tested compound on hematological parameters of mice.

Ehrlich ascites carcinoma respectably < 0.05) diminished count (RBCs); (P hemoglobin (Hb) concentration is compared to the negative control group. Moreover, Ehrlich ascites carcinoma slightly (P >0.05) decreased in platelets (PLT) count, neutrophil and monocyte compared to the negative control group, while white blood cells (WBCs) count and lymphocyte were slightly increased (p >0.05) in the EAC-bearing group compared to the negative control group. In contrast, treatment of mice inoculated with EAC with the tested compound for 2 weeks after induction of EAC highly significantly (p < 0.01) increased RBCs count, HGB concentration and slightly increased (p > 0.05) white blood cells (WBCs) count, PLT count, lymphocytes and monocytes in comparison with the EAC bearing group, while neutrophils (p < 0.05) significantly decreased, is compared to the EAC-bearing group in Table 1.

Table 1: Effect of the tested compound on hematology profile in various estimated groups.

Item	Group 1 Negative control	Group 2 DMSO	Group 3 Drug control	Group 4 the EAC-bearing group	Group 5 Therapeutic
Hemoglobin (g/dl) (mean $\pm$ SD)	$13.04\pm3.28$	13.37 ±1.55	$12.30 \pm 1.37$	10.42 ±1.39*	$12.288 \pm 1.04$
RBCs (x100 <sup>3</sup> cells/ $\mu$ l) (mean $\pm$ SD)	9.74 ±2.62	13.38 ±1.55	$9.70 \pm 1.07$	7.45 ±0.87	11.9±0.2**
WBCs( $x10^3$ /mm <sup>3</sup> ) (mean ± SD)	$5.48 \pm 1.97$	$6.33 \pm 1.01$	$11.60 \pm 3.06$	5.8 ±0.5	$6.94 \pm 1.21$
PLT( $x10^{3}/mm^{3}$ ) (mean $\pm$ SD)	$578 \pm 258.70$	$483 \pm 298.76$	$646 \pm 36.40$	$334 \pm 97.82^*$	$679 \pm 195.00^{*}$
Neutrophils % (mean ± SD)	7.8 ±0.95	5.72±0.33	$4.50 \pm 0.4$	2.86±0.27**	6.5 ±0.65**
Lymphocytes % (mean ± SD)	$78.5 \pm 1.58$	79.1 ±2.45	$83.12 \pm 2.69$	68.0 ±3.39**	$84.48 \pm 1.24^{**}$
Monocytes % (mean ± SD)	13.7±0.7	$16.10 \pm 2.58$	12.3±2.83	23.1 ±3.55**	9.02 ±1.43**

Therapeutic group was in comparison with the positive control group (EAC bearing group). Therapeutic and positive groups were in comparison with the negative control group.

\* P value<0.05 was considered significant. \*\* P value<0.01 was considered highly significant.

#### Changes in hepatic function tests

The serum glutamic pyruvic transaminase (SGPT) activity's mean value of the negative control group was  $13.4\pm 2.7$  (U/L). This value of the drug group was marginally raised to  $14.1\pm 2.57$  (U/L) (P > 0.05) and the EAC-bearing group's value was highly considerably raised to  $98.6 \pm 7.4$  (U/L) (P < 0.01). When compared to the EAC-bearing group, the therapy group's ALT activity decreased by a very significant amount during treatment, to  $20.0\pm 1.6$  (U/L) (P< 0.01). in Figure 2b.

The serum glutamic oxaloacetic transaminase (SGOT) activity's mean value of the negative control group was  $44.5\pm 5.7$  (U/L). This value of the drug group was mild declined to  $35.0\pm 9.8$  (U/L) (P > 0.05) and the EAC-bearing group's value was extremely significant raised to  $425.00\pm 60.0$  (U/L) (P < 0.01). When the test compound was used in therapy, the activity of AST decreased to  $12.4\pm 2.9$  (U/L) (P < 0.01) for the treatment group as opposed to the EAC-bearing group in a very respectable manner in Figure 2a.

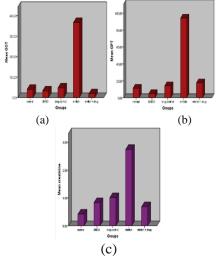


Figure 2: Effect of the tested compound on liver and kidney function tests in various estimated groups: (a) ALT activities's mean. (b) AST activities's mean. (c) Creatinine concentrations's

#### Changes in renal function tests

The creatinine concentration's mean value of the negative control group was  $0.4\pm 0.02 \text{ (mg/dL)}$ . This value of the drug group was extremely considerably elevated to  $1.0\pm 0.2 \text{ (mg/dL)}$  (P < 0.01) and the EAC-bearing group's value was extremely considerably elevated to  $2.72\pm 0.50 \text{ (mg/dL)}$  (P < 0.01). When comparing the therapy group to the EAC carrying group, the evaluated chemical therapy significantly reduced the creatinine concentration to  $0.6\pm 0.2 \text{ (mg/dL)}$  (P < 0.01) in Figure 2c.

#### Changes in antioxidant assays

In Table 2, The total antioxidant capacity (TAC)'s mean value of the negative control group in the hepatic tissue was  $0.75\pm0.04$  (mM/L). This value of the drug group was mild declined to  $0.71\pm0.04$  (mM/L) (P >0.05) and the EAC-bearing group's value was extremely considerably diminished to  $0.33\pm0.02$  (mM/L) (P < 0.01). When compared to the EAC-bearing group, the treated group's total antioxidant capacity in the hepatic tissue increased significantly after therapy with the evaluated chemical, reaching  $0.70\pm0.05$  (mM/L) (P < 0.01).

The malondialdehyde (MDA)'s mean value of the negative control group in the hepatic tissue was  $3.35\pm1.21$  (nmol/g. tissue). This value of the drug group was mild declined to  $3.00\pm0.27$  (nmol/g. tissue) (P > 0.05) and the EAC-bearing group's value was considerably elevated to  $6.59\pm3.55$  (nmol/g. tissue) (P < 0.05). When compared to the EAC-bearing group, the treated group's MDA in the hepatic tissue decreased significantly to  $3.67\pm0.23$  (nmol/g. tissue) (P < 0.05) after treatment with the studied drug.

Table 2: The changes of antioxidant levels in liver tissues in various estimated groups.

	Group 1	Group 2	Group 3	Group 4	Group 5
Test	Negative control	DMSO	Drug control	The EAC-bearing group	Therapeutic
MDA (mean±SD)	3.35±1.21	4.15±1.7	3.00±0.27	6.58±3.54*	3.67±0.23*
TAC (mean±SD)	0.75±0.04	1.57±0.20	0.71±0.04	0.33±0.02**	$0.70\pm0.05^{**}$

Therapeutic group was in comparison with the positive control group (EAC bearing group). Therapeutic and positive groups were in comparison with the negative control group.

\* P value<0.05 was considered significant.

\*\* P value<0.01 was considered highly significant.

		GOT	GPT	MDA	TAC	Hb	WBCs
GOT	Pearson Correlation	1	.964**	.503*	571 **	438 *	270
	Sig. (2-tailed)		.000	.010	.003	.028	.193
	N	25	25	25	25	25	25
	Pearson Correlation	.964**	1	.618**	652 **	508 **	256
GPT	Sig. (2-tailed)	.000		.001	.000	.009	.216
	N	25	25	25	25	25	25
	Pearson Correlation	.503*	.618**	1	202	302	322
MDA	Sig. (2-tailed)	.010	.001		.333	.142	.117
	N	25	25	25	25	25	25
	Pearson Correlation	571 **	652 **	202	1	.423*	080
TAC	Sig. (2-tailed)	.003	.000	.333		.035	.703
	N	25	25	25	25	25	25
Hb	Pearson Correlation	438 *	508 **	302	.423*	1	.010
	Sig. (2-tailed)	.028	.009	.142	.035		.964
	N	25	25	25	25	25	25
WBCs	Pearson Correlation	270	256	322	080	.010	1
	Sig. (2-tailed)	.193	.216	.117	.703	.964	
	N	25	25	25	25	25	25

Table 3: Pearson's correlation analysis between GOT, GPT, MDA, TAC, Hb and WBCs in all studied groups.

\*\*. Correlation is significant at the 0.01 level (2-tailed).

\*. Correlation is significant at the 0.05 level (2-tailed).

Table 4: Pearson's correlation analysis between WBCs, neutrophils, lymphocytes and monocytes in all studied groups.

		MDA	TAC	WBCs	neutrophils	Ly11mphocytes	monocytes
	Pearson Correlation	1	-0.202	-0.322	-0.396	-0.599 **	$0.479^{*}$
MDA	Sig. (2-tailed)		0.333	0.117	0.050	0.002	0.015
	N	25	25	25	25	25	25
	Pearson Correlation	-0.202	1	-0.080	.339	0.255	149
TAC	Sig. (2-tailed)	0.333		0.703	0.098	0.218	0.478
	N	25	25	25	25	25	25
	Pearson Correlation	-0.322	-0.080	1	-0.261	$0.459^{*}$	312 0.129
WBCs	Sig. (2-tailed)	0.117	0.703		0.208	0.021	0.129
	N	25	25	25	25	25	25
	Pearson Correlation	-0.396	0.339	261	1	0.506**	-0.621 **
Neutrophils	Pearson Correlation         -0.396         0.339        261         1		0.010	0.001			
- · · · · · · · · · · · · · · · · · · ·	N	25	25	25	25	25	25
	Pearson Correlation	-0.599 **	0.255	$0.459^{*}$	0.506**	1	-0.893 **
Lymphocytes	Sig. (2-tailed)	0.002	0.218	.021	0.010		000
	N	25	25	25	25	25	25
	Pearson Correlation	$0.479^{*}$	-0.149	-0.312	-0.621 **	-0.893 **	1
Monocytes	Sig. (2-tailed)	0.015	0.478	0.129	0.001	000	
	N	25	25	25	25	25	25

\*\*. Correlation is significant at the 0.01 level (2-tailed).

\*. Correlation is significant at the 0.05 level (2-tailed).

#### Discussion

From a morbidity and mortality perspective, cancer is the most common and well-known threat to general health (Tuktibayeva et al., 2023). Numerous biological processes and alterations to cell signaling pathways are among the many elements that influence this pathogenesis (Almatroodi et al., 2020).

The majority of cancer treatments include heterocyclic chemistry. Chemotherapy treatments for cancer represent the greatest

observable advancement in heterocyclic nitrogen compounds (Hosseinzadeh et al., 2018).

The principal purpose of this assayment was to find out if the current compound has antioxidant and anti-tumor effects against the EAC damage or not.

Myelosuppression and anemia are typically the most problematic side effects of cancer chemotherapy (Han et al., 2023). The main cause of anemia in EAC-bearing mice is the decrease in the percentage of red blood cells (RBCs) or hemoglobin. Hemolytic or myelopathic illnesses, as well as insufficient iron intake, can also cause anemia (Rausch et al., 2021). Hemoglobin, red blood cell count, and white blood cell count were all mostly restored to normal following treatment with the tested chemical. This demonstrated the protective impact of the tested drug on the hematological profile.

Proteins, lipids, nucleic acids, and carbohydrates are damaged by oxidation under conditions of oxidative stress, which is resulting from unbalanced concentration an of antioxidants and free radicals (Tamboli and Wadkar 2021). The body has been protected by antioxidants from the negative consequences of free radicals. Natural anti-oxidants boost endogenous antioxidants, which protect against reactive oxygen species, and help to restore the ideal balance by neutralizing the ROS (Tamboli and Wadkar 2021).

The body's creation of free radicals influences several essential physiological functions, including neutrophil and macrophage production of superoxide and nitric oxide, which aid in the process of phagocytosis and aid in the death of microbes by these cells. Free radicals. which are involved in the inflammatory response, also hasten fibroblasts' cellular division (mitosis), allowing scar tissue to develop, and they catalyze lymphocyte proliferation during the creation of clones. Superoxide radicals, which are basically nonselective antibiotics that destroy all invasive bacteria and neutrophils while also having the potential to harm neighboring tissue cells, are produced by phagocytic cells. Moreover, causes vasodilation, which increases blood flow to the inflammatory region, by no relaxing vascular smooth muscle. (Gupta et al., 2004).

In earlier research, ROSs were discovered to contribute to the development and spread of cancer. Patients with tumors had higher MDA concentrations (Rahman et al., 2017). In addition to ROS, oxidative stress can cause isolated lipid peroxidation, which damages DNA and directly inhibits proteins, injuring cells. Malondialdehyde can serve as a proxy for the active peroxidation of lipid because it is a stationary end product of the peroxidation of lipid (Mao et al., 2019).

Our studies agree with Toson et al., 2016 and Zahran et al., 2024 that announced that antioxidants concurrently declining along with MDA's elevation in animals with tumors suggest a condition of oxidative stress, which leads to tissue and cellular damage, including probably damage to hepatocytes and EAC cells.

Total antioxidant capacity in the

hepatic tissue was significantly increased by the studied medication treatment, with values of  $0.70 \pm 0.05$  (mM/L) (P<0.01) compared with EAC-bearing group. According to (Kusuma et al. 2024), Their ability to effectively remove reactive oxygen species (ROS) by direct H-atom donation or single electron transfer (SET) from hydroxyl groups followed by protonation is their primary mode of action. After administering the tested drug, the therapeutic group's MDA in the hepatic tissue diminished respectably to  $3.67 \pm 0.23$  (nmol/g) (P < 0.05) when compared to the EAC-bearing group.

These analyses concur with those of (Kumar et al., 2014), who showed how oxidative stress promotes to the formation of cancer and who found a considerable diminution in the hepatic catalase levels in EAC-bearing mice, along with an increase in MDA. Furthermore, in EAC models, mice administered the test chemical displayed reduced MDA levels and increased catalase levels.

The endogenous antioxidant system effectively utilizes glutathione, a strong inhibitor of the neoplastic process. Elevated concentrations are observed in the liver, an organ recognized for its pivotal function in the immune system. Oxidative stress, brought on by an overabundance of free radical production, breaks down macromolecules like lipid peroxidation in vivo (Sannigrahi et al., 2010). The existence of cancers in humans or experimental animals is known to impact a variety of essential organ functions, including those of the liver, even in cases when the tumor site does not directly alter organ function (Anthony et al., 2023). The anti-cancer chemical characteristics of the under investigation may have been attributed to decreased lipid peroxidation and elevated catalase levels. As a result, the investigated chemical's anti-cancer characteristics may be linked to its in vivo antioxidant characteristics.

Hepatic assignments are indicated by liver enzymes like GOT and GPT. Normal hepatic cell metabolism is often disrupted by liver damage brought on by tumor cells, resulting in variations in the serum enzyme activity (Aldubayan et al., 2019).

Our consequences work in with (Sankhe et al., 2019), who showed that increasing ALT and AST levels were evidence of HCC in a number of animal studies. The increased GOT and GPT levels have been

linked to liver injury or alterations in membrane permeability, indicating that Ehrlich tumors severely harm hepatic cells (Sankhe et al., 2019). This increase in AST and ALT activity was severely impaired by treatment with the tested compound. Our results showed that therapy with the tested compound showed a very significant decrease in AST activity to 12.4  $\pm$  2.9 (U/L) (P < 0.01) for the therapeutic group compared to the EAC-bearing group. Furthermore it, therapy with the tested compound showed a very respectable decrease in ALT activity to 20  $\pm$  1.6 (U/L) (P < 0.01) for the treatment group, compared to the EACbearing group.

For the early detection and ongoing monitoring of kidney disease, as well as the preventive admission of renal failure, reliable laboratory testing of kidney function is essential. These outcomes are convenient for (Mutar et al., 2020) and (Ezeldien et al., 2019) Who claimed that Ehrlich tumors had an unsettling impact on mice's biochemical parameter creatinine, causing kidney damage, severe changes in renal function, and elevated level of creatinine.

#### Conclusion

In the present study, we concluded that the tested compound acts as an anti-oxidant compound with hepatoprotective and nephroprotective properties, so it can be used as anti-tumor drug. So, more studies on the tested compound should be conducted to confirm its efficacy.

List of Abbreviations

Ehrlich ascites carcinoma
Serum glutamic pyruvic transaminase
Serum glutamic oxalo acetic transaminase
Total antioxidant capacity
Melanoaldehyde

# Declaration

#### Ethics approval and consent to participate

All described experimental procedures were reviewed and approved by the Research Ethics Committee at Faculty of Medicine, Benha University, Egypt (RES-FOMBU). Permit No. (MS.21.3.2023). All experiments were performed according with all relevant guidelines and regulations including the ARRIVE guidelines.

## **Consent for publication**

Not applicable

## Availability of data and materials

The datasets used and /or analyzed during the current study are available from the corresponding author on reasonable request.

## **Competing inerests**

The authors state that they do not have any competing interests.

# Funding

The authors affirm that they did not accept any funds, grants, or other assistance for the creation of this manuscipt.

#### **Authors contributions**

R.F.Z, R.M.E M.A.D and conceptualized conducted and experiments.;R.F.Z,R.M.E M.A.D and aided in the evaluation and /or explication of data. R.F.Z,R.M.E and M.A.D drafted the manuscript and R.F.Z.R.M.E and M.A.D reseived it for significant logical content. The manuscript has been read and approved by all of the authors.

# Acknowledgment

We would like to thank all of authors who contributed to this study and helped to carry out it.

#### References

Abd Eldaim, Mabrouk Attia, Ehab Tousson, Ibrahim El Tantawy El Sayed, Asmaa Zakaria Abd Elmaksoud, and Abdullah AS Ahmed. 2021. 'Ameliorative effects of 9-diaminoacridine derivative against Ehrlich ascites carcinomainduced hepatorenal injury in mice', *Environmental Science and Pollution Research*, 28: 21835-50.

- Agrawal, Shyam S, Sarita Saraswati, Rajani Mathur, and Maneesha Pandey. 2011. 'Antitumor properties of Boswellic acid against Ehrlich ascites cells bearing mouse', *Food and Chemical Toxicology*, 49: 1924-34.
- Aldubayan, Maha A, Rehab M Elgharabawy, Amira S Ahmed, and Ehab Tousson. 2019. 'Antineoplastic activity and curative role of avenanthramides against the growth of ehrlich solid tumors in mice', Oxidative medicine and cellular longevity, 2019.
- Almatroodi, Saleh A, Ahmad Almatroudi, Amjad Ali Khan, Fahad A Alhumaydhi, Mohammed A Alsahli, and Arshad Husain Rahmani. 2020. 'Potential therapeutic targets of epigallocatechin gallate (EGCG), the most abundant catechin in green tea, and its role in the therapy of various types of cancer', *Molecules*, 25: 3146.
- Anthony, Reshma M, Madison D Amundson, John Brejda, and Iveta Becvarova. 2023. 'Acceptance of a Novel, Highly Palatable, Calorically Dense, and Nutritionally Complete Diet in Dogs with Benign and Malignant Tumors', *Veterinary Sciences*, 10: 148.
- Bashiri, Mohammad, Aliasghar Jarrahpour, S Masoud Nabavizadeh, Somaye Karimian, Banafsheh Rastegari, Elahe Haddadi, and Edward Turos. 2021. 'Potent antiproliferative active agents: novel bis Schiff bases and bis spiro  $\beta$ -lactams bearing isatin tethered with butylene and phenylene as spacer and DNA/BSA binding behavior as well as studying molecular docking', *Medicinal Chemistry Research*, 30: 258-84.
- Bindhu, S, KL Pramod, and Ashaiba Asiamma. 2023. 'Effect of valeric acid on the neurotransmitter levels of hippocampus on Alzheimer's induced rats', *Biomedicine*, 43: 625-29.
- Brągoszewska, Ewa, Izabela Biedroń, and Wojciech Hryb. 2020. 'Microbiological Air Quality and Drug Resistance in Airborne Bacteria Isolated from a Waste Sorting Plant Located in Poland—A Case Study', *Microorganisms*, 8: 202.
- Dayem, Ahmed Abdal, Hye-Yeon Choi, Jung-Hyun Kim, and Ssang-Goo Cho. 2010. 'Role of oxidative stress in stem, cancer, and cancer stem cells', *Cancers*, 2: 859-84.
- Doudach, Latifa, Samiah H Al-Mijalli, Emad M Abdallah, Hanae N Mrabti, Fatiha Chibani, and Moulay El Abbes Faouzi. 2022. 'Antibacterial evaluation of the roots of Moroccan Aristolochia longa against referenced Gram-positive and Gram-negative Bacteria', *Advancements in Life*

Sciences, 9: 116-21.

- El-Ansary, Afaf, Naima Zayed, Laila Al-Ayadhi, Hanan Qasem, Mona Anwar, Nagwa A Meguid, Ramesa Shafi Bhat, Monica Daniela Doşa, Salvatore Chirumbolo, and Geir Bjørklund. 2021. 'GABA synaptopathy promotes the elevation of caspases 3 and 9 as pro-apoptotic markers in Egyptian patients with autism spectrum disorder', *Acta Neurologica Belgica*, 121: 489-501.
- El-Sonbati, AZ, MA Diab, RA Elfayoumy, AM Eldesoky, and SA El-Sayad. 2022. 'Synthesis, Characterization, Electrochemical Studies and Biological Activities of Complexes of Tridentate Schiff Base Ligand with Divalent Metal Ions', *Egyptian Journal of Chemistry*, 65: 51-72.
- Ezeldien, S, WF Khalil, M Fayez, and MM Abdel-Daim. 2019. 'Chloroquine and gemifloxacin potentiate the anticancer effect of doxorubicin: in-vitro and in-vivo models', *Biomedical & Pharmacology Journal*, 12: 1613-20.
- García, María del Carmen, Patricia Pazos, Luis Lima, and Carlos Diéguez. 2018. 'Regulation of energy expenditure and brown/beige thermogenic activity by interleukins: new roles for old actors', *International Journal of Molecular Sciences*, 19: 2569.
- Gupta, Malaya, Upal Kanti Mazumder, Ramanathan Sambath Kumar, Thangavel Sivakumar, and Madgula Lakshmi Mohan Vamsi. 2004. 'Antitumor activity and antioxidant status of Caesalpinia bonducella against Ehrlich ascites carcinoma in Swiss albino mice', *Journal of Pharmacological Sciences*, 94: 177-84.
- Hameed, Shahad Imad, Rand H Alwakeel, and Ayyad W Al-Shahwany. 2022. 'Comparative Study between a Combination of Plants Extracts and Drugs on Thyroid Hormones and Lipid Profile in Experimental Animals', *INTERNATIONAL JOURNAL OF SPECIAL EDUCATION*, 37.
- Han, Jiahong, Xuan Fei, Nian Sun, Junjia Xing, Enbo Cai, and Limin Yang. 2023. 'Effect of Ligustri Lucidi Fructus on myelosuppression in mice induced by cytoxan', *Biomedical Chromatography*, 37: e5524.
- Ho, Li-Kang, Ming-Jaw Don, Hua-Chien Chen, Sheau-Farn Yeh, and Jau-Ming Chen. 1996.
  'Inhibition of hepatitis B surface antigen secretion on human hepatoma cells. Components from Rubia cordifolia', *Journal of natural products*, 59: 330-33.
- Hosseinzadeh, Zahra, Ali Ramazani, and Nima Razzaghi-Asl. 2018. 'Anti-cancer nitrogencontaining heterocyclic compounds', *Current Organic Chemistry*, 22: 2256-79.
- Hrubisko, M, L Sanislo, M Zuzulova, J Michalickova, T Zeleznikova, J Sedlak, and V

Bella. 2010. 'Immunity profile in breast cancer patients', *Bratislavske lekarske listy*, 111: 20-26.

- Hsu, Hsi-Hsien, Wei-Wen Kuo, Cecilia Hsuan Day, Marthandam Asokan Shibu, Shin-Yi Li, Sheng-Huang Chang, Hui-Nung Shih, Ray-Jade Chen, Vijaya Padma Viswanadha, and Yueh-Hsiung Kuo. 2017. 'Taiwanin E inhibits cell migration in human LoVo colon cancer cells by suppressing MMP-2/9 expression via p38 MAPK pathway', *Environmental toxicology*, 32: 2021-31.
- Kumar, Nitesh, Isha Dhamija, P Vasanth Raj, BS Jayashree, Vipan Parihar, SN Manjula, Seeja Thomas, N Gopalan Kutty, and C Mallikarjuna Rao. 2014. 'Preliminary investigation of cytotoxic potential of 2-quinolone derivatives using in vitro and in vivo (solid tumor and liquid tumor) models of cancer', *Arabian Journal of Chemistry*, 7: 409-17.
- Kusuma, Ikhwan Yuda, Habibie Habibie, Muh Akbar Bahar, Ferenc Budán, and Dezső Csupor. 2024. 'Anticancer Effects of Secoiridoids—A Scoping Review of the Molecular Mechanisms behind the Chemopreventive Effects of the Olive Tree Components Oleocanthal, Oleacein, and Oleuropein', *Nutrients*, 16: 2755.
- Mao, Chen, Jin-Qiu Yuan, Yue-Bin Lv, Xiang Gao, Zhao-Xue Yin, Virginia Byers Kraus, Jie-Si Luo, Choy-Lye Chei, David Bruce Matchar, and Yi Zeng. 2019. 'Associations between superoxide dismutase, malondialdehyde and all-cause mortality in older adults: a community-based cohort study', *BMC geriatrics*, 19: 1-9.
- Meeker, John D, Louise Ryan, Dana B Barr, and Russ Hauser. 2006. 'Exposure to nonpersistent insecticides and male reproductive hormones', *Epidemiology*: 61-68.
- More, Veena, Abdullatif Bin Muhsinah, GS Latha, Abdulfattah Yahya M Alhazmi, Osama Abdulaziz Ibrahim, Abdulkarim S. Binshaya, Mater H Mahnashi, Hassan H Almasoudi, Harshitha Gangadharappa, and Sahana Nagappa Maruthi. 2022. 'Evaluation of Anti-Venom Potential of Areca catechu Seed Extract on Bungarus caeruleus Venom', *Separations*, 9: 360.
- Mutar, Thulfiqar F, Ehab Tousson, Ezar Hafez, Maha Abo Gazia, and Seham B Salem. 2020. 'Ameliorative effects of vitamin B17 on the kidney against Ehrlich ascites carcinoma induced renal toxicity in mice', *Environmental toxicology*, 35: 528-37.
- Okamoto, Masami. 2023. 'Polymer nanocomposites', *Eng*, 4: 457-79.
- Omer, Zamzam Taher, Megha Rai, Pravin Chavan, Rashmi Pathrikar, and Shivaji Jadhav. 2021.
  'Design and Development of Complexation of Ce Metal Ions with Synthesized INZ Incorporated Bio-active Schiff Bases'.

- Rahman, Mohammad Saifur, Mohammad Badrul Alam, Yun Hee Choi, and Jin Cheol Yoo. 2017. 'Anticancer activity and antioxidant potential of Aponogeton undulatus against Ehrlich ascites carcinoma cells in Swiss albino mice', *Oncology letters*, 14: 3169-76.
- Rausch, Valentina, Valentina Sala, Fabio Penna, Paolo Ettore Porporato, and Alessandra Ghigo. 2021. 'Understanding the common mechanisms of heart and skeletal muscle wasting in cancer cachexia', *Oncogenesis*, 10: 1.
- Saleem, Muhammad Farrukh, Mohsin Abbas Khan, Irshad Ahmad, Naveed Aslam, and Umair Khurshid. 2021. 'Synthesis and characterization of some new Schiff base derivatives of gabapentin, and assessment of their antibacterial, antioxidant and anticonvulsant activities', *Tropical Journal of Pharmaceutical Research*, 20: 145-53.
- Sankhe, Neena M, Ega Durgashivaprasad, N Gopalan Kutty, J Venkata Rao, K Narayanan, Nitesh Kumar, Prateek Jain, Nayanabhirama Udupa, and P Vasanth Raj. 2019. 'Novel 2, 5disubstituted-1, 3, 4-oxadiazole derivatives induce apoptosis in HepG2 cells through p53 mediated intrinsic pathway', *Arabian Journal of Chemistry*, 12: 2548-55.
- Sannigrahi, Santanu, Upal Kanti Mazumder, Arijit Mondal, Dilipkumar Pal, Silpi Lipsa Mishra, and Souvik Roy. 2010. 'Flavonoids of Enhydra fluctuans exhibit anticancer activity against Ehrlich's ascites carcinoma in mice', *Natural Product Communications*, 5: 1-9.
- Sun, Cuixiang, Diana K Hunt, Roger B Clark, Denene Lofland, William J O'Brien, Louis Plamondon, and Xiao-Yi Xiao. 2011. 'Synthesis and antibacterial activity of pentacyclines: a novel class of tetracycline analogs', *Journal of medicinal chemistry*, 54: 3704-31.
- Tamboli, Ashpak M, and Kiran A Wadkar. 2021. 'Anticancer activity of leaves extracts of Convolvulus pluricaulis and Mimosa rubicaulis (Lam.) by Brine Shrimp Lethality Bioassay', *Research Journal of Pharmacy and Technology*, 14: 5427-32.
- Tassa, Bikram Dutta, Navajit Sahu, Nabajit Barman, and Gautam Sahu. 2023. 'Antihyperlipidemic and Antioxidant Activities of Ethanolic Extract of Paederia foetida Leaves (EEPFL) in Albino Rats'.
- Toson, El-Shahat A, Fahed M Almutairi, Amira Ali Elfalal, Salem A Habib, Rasha F Zahran, and Mohamed Elbakry. 2016. 'Suppression Effect of Superoxide Dismutase (SOD)-Like Activity Protein Partially Purified from Raphnus sativus Leaves against Liver Metastasis in Mice Intraperitoneally Infected with Ehrlich Ascites Carcinoma Cell', *Natural Science*, 8: 321-32.

- Tuktibayeva, S, S Alipbekova, B Omarova, Beisenbayeva Zh, A Tursunbekov, B Yessenbekov, K Kenessova, and K Kemelbekov.
  2023. 'The Level And Dynamics Of Morbidity By The Main Classes Of Diseases And Their Prediction In The Able-Bodied Population Of The Turkestan Region', *Journal of Population Therapeutics and Clinical Pharmacology*, 30: 431-41.
- Tuo, Qing-zhang, Shu-ting Zhang, and Peng Lei. 2022. 'Mechanisms of neuronal cell death in ischemic stroke and their therapeutic implications', *Medicinal Research Reviews*, 42: 259-305.
- Willcox, Joye K, Sarah L Ash, and George L Catignani. 2004. 'Antioxidants and prevention of chronic disease', *Critical reviews in food science and nutrition*, 44: 275-95.
- Zahran, R F, Rady, G M and El-Sonbati, AZ. 2024. Evaluation of antioxidant and anti-inflammatory activities of 4-((quinolin-2-yl) methyleneamino)-1,2-dihydro-2,3-dimethyl-1-phenylpyrazol-5one on Ehrlich ascites carcinoma bearing mice', *Scientific Journal for Damietta Faculty of Science*, 14(2): 1-12. doi: 10.21608/sjdfs.2024.312894.1176.

الملخص العربى

# عنوان البحث: تأثير ١-((٢-هيدروكسي فينيل) إيمينو ميثيل)-٢- نافثول على المؤشرات الكيميانية الحيوية والدموية في الفئران الحاملة لخلايا إيرليش السرطانية

رشا فكري زهران (\*، رحمة محمد السقا ، مصطفى أمين دياب ً

اشعبة الكيمياء الحيوية – قسم الكيمياء – كلية العلوم – جامعة دمياط – مصر. اقسم الكيمياء – كلية العلوم – جامعة دمياط – مصر.

تعتبر المركبات التي تحتوي علي قواعد شيف من اهم المركبات التي تدخل ف العلاج الكيماوي لعلاج مختلف انواع مرض السرطان ومن ضمن هذه المركبات مركب [١-((٢-هيدروكسي فينيل)امينو ميثيل) ٢-نافثول ] وهو المركب الذي تم دراسته في هذا البحث من حيث تأثيره على الوظائف الكيميائية الحيوية وتأثيره كمضاد اكسدة وبالتالي يكون له تأثيرا مضاد للسرطان.

خطوات العمل : تم تقسيم مجموعة من ذكور الفئران الصغيرة السويسرية التي خمس مجموعات حيث تمثل كل مجموعة خمس وعشرون فارا، المجموعة الاولي: تم حقنها بمحلول ملحي ، المجموعة الثانية تم حقنها بمحلول الداي ميثيل سالفو أوكسيد ،المجموعة الثالثة : تم حقنها اليوم الاول فقط بخلايا ايرلش السرطانية ،المجموعة الرابعة: وهي التي تم حقنها بالعلاج فقط لمدة ٤ أيوم متتالي و المجموعة الخامسة :تم حقن فئر ان تحمل خلايا ايرلش بالعلاج لمدة ٤ أيوم وبعد ذلك تم سحب عينات دم لدر اسة الوظائف الحيوية الكيميائية وتاثير العلاج المضاد للاكسدة.

النتائج:ارتفاع غير طبيعي للوظائف الحيُّوية في الفئران الحاملة لخلايا ايرلش

وبعد علاج الفئران الحاملة لخلايا ايرلش بالمركب محل الدراسة وجدنا ان مستوي الوظائف الحيوية قريبة جدا من مستواها الطبيعي بالاضافة الي ارتفاع التاثير المضاد للاكسدة .

الخلاصة : تشير النتآنج الي آن هذا المركب له تاثير مضاد تاكسدي وكذلك تاثيره الفعال في تحسن مستوي الوظائف الحيوية الناتجة عن خلايا ايرلش السرطانية ولذلك يمكن استخدامه كمضاد للسرطان.