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Green Synthesis of Mg Nanoparticles Using Ocimum Basilicum (ObE-MgNPs): Characterization, Acute Toxicity Evaluation and Hepato-Protective against Side Effect of Doxorubicin Chemotherapy in Rats

Islam Boulaares[1,2], Samir Derouiche[1,2], Imane Yousra Guemari[1]

[1]Department of Cellular and Molecular Biology, Faculty of the Sciences of Nature and Life, El-Oued University, El-Oued 39000, El Oued, Algeria

[2]Laboratory of Biodiversity and application of biotechnology in the agricultural field, Faculty of the Sciences of Nature and Life, University of El Oued, El-Oued 39000, Algeria

ABSTRACT: This investigation was aimed to evaluation of Doxorubicine a chemotherapy substance induced hepatotoxicity and the preventive effect of ObE-MgNPs in rats. Standard procedures were used to extract bioactive molecules and test qualitative phytochemical substances. Furthermore, visual observation, FT-IR spectroscopy, and scanning electron microscopes (SEM), techniques were used to verify the green synthesis of ObE-MgNPs. For in-vivo rats study, 15 female albino Wistar rats were divided into 3 groups (n = 5); control group, doxorubicin treated rats group (DOX) and rats co-treated with doxorubicin and MgNPs group (DOX + MgNPs). Various hematological, enzymatic, and oxidative stress markers were estimated. The FT-IR spectroscopy analysis confirmed the synthesis of SeNPs and scanning electron microscope (SEM) analysis revealed the spherule-like structure of MgNPs with average size around 78.5 nm. Phytochemical results appeared the richness of Ocimum basilicum L. extract by various phenolic compounds. In in-vivo study results show that doxorubicin induce an alteration in hematological parameters and enzymatic activities compared to control group. In addition, doxorubicin treated rats induced oxidative stress in liver cells compared to control rats. Co-treatment of doxorubicin with MgNPs were partially reversed all of previous parameters. This study indicated that the antioxidant property of Magnesium nanoparticles allowed using them to protect organs from the side effects of doxorubicin or from the destructive effects of various diseases.

KEYWORDS: MgNPs, Ocimum basilicum, Hepatotoxicity, Doxorubicin, Oxidative stress, Rat

1. INTRODUCTION

Cancer is a group of diseases causing change in body cells and proliferates beyond of control [1]. Cancer is a major public health problem worldwide [2], and the second leading cause of death after cardiovascular diseases [3]. There are many cancer treatments, the most important of which are chemotherapy that considered the most effective and extensively used modality in most types of cancers [4]. Doxorubicin is an anthracycline glycoside antitumor antibiotic used as a first-line drug in combination with other chemotherapy drugs for various types of cancers [5]. Unfortunately, doxorubicin also can induce toxic and side effects in many organs, compromising its usage and efficacy [6]. According to Zhao et al. (2022), the liver is the first and most vulnerable organ to poisons as a crucial organ for detoxification and digesting. It is a crucial metabolic organ in the body that secretes bile and converts various nutrients into proteins [7]. The liver transforms, neutralizes, and eliminates toxins using hepatocyte-mediated enzymatic detoxification mechanisms, which is the primary method of tissue detoxification [8].

Nanotechnology is an area of emerging interest in the field of science and technology due to its wide variety of applications in the field of biomedicine, optics, and electronics [9]. Nowadays, nanotechnology involving green synthesis of nanoparticles has become an eye-catching idea [10]. Recently, plant-mediated route or green approach for preparing metal and metal oxide nanoparticles has received enormous attention due to the ease of preparation and environmental friendliness when compared to physical and chemical methods [11]. Biosynthesis of nanoparticles using plant extracts is gaining importance in biomedical applications because of their unique properties [12]. The objective of the present study to assess the hepatotoxicity effects of doxorubicin and to study the protective effects of therapeutic systems based on green synthesis of Magnesium nanoparticles in female Wistar albino rats.

2. MATERIALS AND METHODS

2.1. Phytochemical analysis

Phytochemical tests were carried out on the aqueous extracts by techniques of qualitative characteristics, according to the standard methods.

Biosynthesis of magnesium oxide nanoparticles

After adding about 5 g of magnesium nitrate (Mg(NO3)2 • 6 H2O) to the plant extract solution, it was heated to 80°C for four hours while being constantly stirred. Using an extract from the leaves of Ocimum basilicum, the magnesium nitrate ions were converted to magnesium oxide or magnesium nanoparticles. The solution's colour changes from yellow to a yellowish-brown hue, signifying the development of magnesium oxide nanoparticles (MgONPs) [13].

2.2. Characterization of the Mg nanoparticles

Analytical techniques were used to characterise the MgONPs that were produced using the aforementioned procedure. Using the Fourier transform infrared spectrophotometer (vector 22, Bruker, Germany), FTIR analysis of magnesium oxide nanoparticles that were biosynthesized was recorded under identical conditions, with a resolution ranging from 400 to 4000 cm−1. Furthermore, scanning electron microscopy (SEM) was used to determine the size and shape of nanoparticles.

2.3. Animal care and experimental design

Our study carried out on 30 female Wistar rats, from the Pasteur Institute of Algiers, aged 8 weeks with a weight of 184.84 ± 8.48 g. The animals are bred at the pet store in the Faculty of Natural and Life Sciences, at Echahid University Hamma Lakhdar-El-Oued. The animals were carried under the same conditions, a period of adaptation (15 days), photoperiod (12h of light/12h of black), at room temperature. The rats are housed in plastic cages and have free access to water and food by a standard diet. The experiment was conducted over a period of 4 weeks.

After a period of adaptation, the animals were divided into 3 experimental groups of 5 animals each as follows:

Group 1 (Control): were normal rats inoculated with physiological saline (one dose/week,

1.5 ml/kg) for 4 weeks.

Group 2 (DOX): Drug control was injected by DOX (one dose/week, 1.5 ml/kg)

for 4 weeks.

Group 3 (DOX + MgNPs): Rats were inoculated with Doxo (one dose/week, 1.5 ml/kg) and

MgNPs (one dose/week, 50 mg/kg) for 4 weeks

Doxorubicin dose induced cardiotoxicity used in this study is according to study of Al Qahtani et al., [14] .

2.4. Sacrifice, blood sampling and tissues collection:

After 16 h of fasting these animals were sacrificed under slight anesthesia by chloroform (94%) by inhalation; blood samples were collected during the slaughter of animals into dry tubes. The serum was obtained by centrifugation for 10 min at 3000 tour/min and used for enzymatic activity analysis. The liver was carefully sampled, washed with normal saline (NaCl) then weighted and stored at -20°c for oxidative stress.

2.5. Enzymatic activities and Hematological markers analysis

Serum enzymatic activities of alanine aminotransferase (GPT), aspartate aminotransferase (GOT), creatine phosphokinase (CPK) and lactate dehydrogenase (LDH) were measured using commercial kits (Spinreact) (refs: GPT-1001171, GOT-1001161, CPK-1001217 and LDH-1001260). The hematological analysis (FNS) is performed by the hematology autoanalyzer (Sysmex).

2.6. Oxidative stress parameters:

About 1g of liver was homogenized in 9 ml of buffer solution of Tris buffer saline (pH=7.4). Homogenates were centrifuged at 4000xg for 20 min +4C° and the obtained supernatant was used for the determination of antioxidant activity. MDA was measured according to the method described by Sastre et al., [15]. The level of reduced Glutathion is determined according to Weckbecker & Cory [16]. About the assay method of SOD activity which using the NBT by the superoxide anion ($O^{2\cdot}$), is used as a basis for detecting of presence of SOD by measuring the spectrophotometrically absorbance at 560 nm [17]. The method used in this study to measure the GSTs is that of Habig et al., [18].

2.7. Statistical analysis

The values of the results were expressed as a percentage or an average ± ES (standard deviation). Student's t-test of independent samples was used. All data in this study were examined by Minitab 13.0 software. $P < 0.05$ indicates statistically significant difference.

3. RESULTS

3.1. Qualitative phytochemical analysis of Ocimum basilicum L

Results of phytochemical essays shows that aqueous extract of Ocimum basilicum L very rich on different important chemical compounds such as flavonoids, steroids, Phenols, Catechic Tannin, Saponoside, Carbohydrate and Alkaloid but our extract plant is poured from Steroids derivatives (Table 01).

Table 1: Phytochemical essays of aqueous extract Ocimum basilicum L

Phytochemical composition	Ocimum basilicum L
Flavonoids	+
Unsaturated steroids	+++
Steroids derivatives	- - -
Phenols	+++
Catechic Tannin	+++
Saponoside	+++
Carbohydrate	+++
Alkaloid	+++

(+): Present (-): Absent

3.2. Characterization of the Mg nanoparticles

The functional group of MgO nanopowder was analyzed by FTIR spectrophotometer in the range 400–4000 cm–1 vibration of the Mg─O bond indicate the presence of magnesium oxide nanoparticles (MgO). The size of the Mg NPs was analyzed through scanning electron microscopy (Figure 2). The absorption bands for MgO nanopowder were 3353, 1644.8, 1362.06, 818.40, and 602.61 cm^{-1}. An sharp peak on the wave number 1352.06 cm^{-1} due to th (SEM) images (Figure…). The size of some selected biosynthesized nanoparticles was 49.2–69.3 nm according to SEM images .

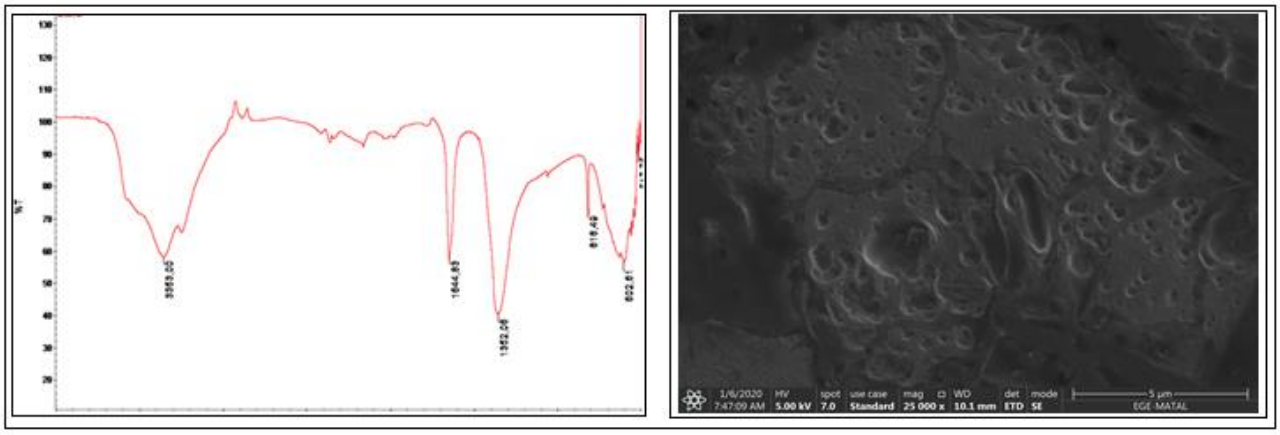

Figure 2: Infrared spectrum and scanning electron microscopy of MgNPs

3.3. Acute toxicity essays of MgNPs

In this experiment, the acute toxicity test was performed on albino Wister rats for 24 hours. Our MgNPs is used with dose of 100 mg to 250 mg /kg weight/rats. The results obtained during this test showed that no mortality was observed before24 hours, which suggests the non-toxic nature of these nanoparticles. The other physiological parameters of the rats were also determined during the experimental period and showed that treatment with the aqueous extract of MgNPs caused no symptoms or complications and also no adverse effects in the rats during the treatment period (Table 03)

Table 10: Effect of aqueous extract of MgNPs on physiological parameters of Wister albino rats

	0 mg/ kg					100 mg/ kg					250 mg/ kg				
Parameters	**0h**	**3h**	**7h**	**14h**	**24h**	**0h**	**3h**	**7h**	**14h**	**24h**	**0h**	**3h**	**7h**	**14h**	**24h**
Death rats	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Eyes	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Sleep	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Diarrhea	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

N, Normal

3.4. Enzymatic activities

As shown in (Table **2**), the results of transaminases enzymes activities appeared an increase of GPT but not significantly, counter to diminution highly significant ($p<0.01$) in GOT activities in Doxo group as compared to the control. Also, the results obtained represent a significant increase in serum of LDH with a very highly significant increase in serum of CPK activity in DOX group as compared to the control oneIn addition, a significant decrease ($p<0.001$) in the GPT ($p<0.001$), GOT ($p<0.01$), CPK ($p<0.001$) and LDH ($p<0.05$) activities, in MgNPs group as compared to the Doxo one. And a very highly significant decrease ($p<0.001$) in the ObE, groups as compared to the DOX group.

Table 2. Enzyme activities in control and experimental groups

Paramaters	Control	DOX	DOX+ MgNPs
GPT (UI/l)	47.2±7.68	60±24.70*	29.55±3.92c
GOT (UI/l)	146±15.20	132.5±3.51**	121.7±11.23b
CPK (UI/l)	182.5±1.51	1337±60.38***	305±22.12 c
LDH (UI/l)	1133±137.06	1419±140.37*	1109±65.22a

Data are expressed as mean± SD (n= 6). * $p<0.05$, ** $p<0.01$, *** $p<0.001$: significantly different from control group.[a] $p<0.05$, [b] $p<0.01$, [c] $p<0.001$: significantly different from Doxo group.

3.5. Hematological markers

The results of the hematological markers (Table 3) for the Doxo treated group compared with the control group showed a significant decrease in WBC ($P<0.01$), lymphocyte($P<0.05$), eosinophil ($P<0.01$), basophil ($P<0.001$) and PLT ($P<0.05$) a significant increase in monocyte ($P<0.01$) but neutrophil cells are showed that no significant differences ($P>0.05$). As well, our results demonstrated that there was a significant amelioration in the level of WBC, neutrophil, lymphocyte, in treatment groups than the DOX group. In this study, findings demonstrated that there was a reducing of eosinophil and monocyte in MgNPs groups ($p<0.001$, $p<0.01$) respectively. Furthermore, there is no significant ($P>0.05$) variation in the platlet parameter.

Table 3. Immune cells count levels in control and experimental groups

Paramaters	Control	DOX	DOX + MgNPs
WBC (10^3/ul)	3.43±0.27	2.04±0.44**	2.880±0.26b
Neutophil (10^3/ul)	0.78±0.11	0.55±0.09	1.19±0.093** c
Lymphocyte (10^3/ul)	1.98±0.18	1.03±0.14*	1.446±0.177* a
Monocyte (10^3/ul)	0.04±0.00	0.18±0.06***	0.094±0.0220* b
Eosinophil (10^3/ul)	0.10±0.00	0.06±0.009**	0.022±0.0032*** c
Basophil (10^3/ul)	0.20±0.02	0.04±0.003***	0.066±0.0139***
Platelet (10^3/ul)	896.8±67.4	1232±35.5*	1259.5±15.4***

Data are expressed as mean± SD (n= 6). * $p<0.05$, ** $p<0.01$, *** $p<0.001$: significantly different from control group.[a] $p<0.05$, [b] $p<0.01$, [c] $p<0.001$: significantly different from Doxo group.

3.6. Oxidative stress parameters

Our results (Table **4**) showed that a significant decrease ($p< 0.01$) of GSH level of liver in DOX group as compared to the control. However, the results showed a very highly significant diminution ($p<0.001$) in MgNPs compared to DOX group. About malondialdehyde (MDA) levels, the results appeared a very highly significant raise ($p<0.001$) of the MDA level of liver in DOX group compared to the control and a significant decrease of the MDA level of liver treated by MgNPs, compared to the DOX group. Results of SOD enzyme activity of liver revealed a high significant increase ($p<0.01$) in Doxo group compared to the control. In addition, treatment with MgNPs showed a high significant decrease compared to DOX group. On the other hand, GST activity in liver demonstrated a very high significant decrease ($p<0.001$) in MgNPs compared to DOX group.

Table 4. Liver oxidative stress markers in control and experimental groups.

Paramaters	Control	DOX	DOX + MgNPs
GSH (µmol/g tissue)	6.21±1.5	5.733±0.82**	7.32±0.63[b]
MDA (µmol/g tissue)	16.1±1.32	31.5±5.72**	11.52±2.36***[c]
SOD (UI/mg of prot)	0.39±0.06	1.52±0.039***	0.42±0.005 [c]
GST (nmol/min/mg prot)	0.5±0.003	4.5±0.06**	2.5±0.0052*** [c]

Data are expressed as mean± SD (n= 6). * p<0.05, **p<0.01, ***p<0.001: significantly different from control group.[a] p<0.05, [b]p<0.01, [c]p<0.001: significantly different from DOX group.

4. DISCUSSION

The result of phytochemical screening confirmed the presence of flavonoids, steroids, Phenols, Catechic Tannin, Saponoside, Carbohydrate and Alkaloid in aqueous extracts of the leafs of Ocimum basilicum L. In agreement with Tariq et al., (2016), O. basilicum is a rich source of secondary metabolites such as glycosides, tannins, phenolic compounds, saponins, flavonoids and terpenes. Terpenes are found to exhibit anti-inflammatory activity [19]. While, Flavonoids exert anti-oxidative effects as free radical scavengers and possess therapeutic potential against osteoporosis and even cancer .Moreover, consumption of phenolic compounds reduces the risk of liver disease [20].

Characterization of MgNPs are demonstrated by the results of FTIR and SEM analysis. Using an FTIR spectrophotometer, the functional group of magnesium oxide nanopowder was examined in the 400–4000 cm-1 range. The stretching vibration of C=C is attributed to a band of 1644.80 cm-1 in the FTIR spectra of the biosynthesized magnesium nanoparticles, as per Solabomi et al. [21] that a band at 1633 cm-1 was discovered. The connection between magnesium and oxygen was confirmed by the peaks detected below 800 cm−1 [22]. Observations using scanning electron microscopy shed more light on the size and form of the produced nanoparticles [23]. SEM pictures of several of the biosynthesized nanoparticles in our research show that their sizes were as small as 50 nm. According to the findings of Sushma et al.'s study [24], MgO's SEM analysis revealed a size range of 50–400 nm with particular binding energies.

.In the present study, Doxo induced hepato-toxicity presented by increase in enzymes LDH, CPK and GPT activities which are known as diagnostic marker of liver function and also DOX induce an immunosuppression by the reduction of the immune cells levels (WBC, lymphocyte, eosinophil and basophil) on the other hand. Doxorubicin bioaccumulation induced free radical generation, triggers membrane degradation and disruption of liver, which can lead to elevations of LDH, CPK, ALT and AST [25]. Doxorubicin as chemotherapy treatment possesses several side effects including cardiotoxic, hepatotoxic and suppress the immune system by decreasing the expression level of IL-2, production of the γ-interferon, natural killer (NK) cells, proliferation of lymphocytes, and ratio CD4+/CD8+ [26]. The levels of proinflammatory cytokines, such as IL-1 and TNFα were significantly increased following doxorubicin administration. Doxo-induced hepatotoxicity is also related to increases in oxidative stress and production of reactive oxygen species (ROS) [27]. The major types of cardiotoxicity ROS are superoxide radical (O2-), hydrogen peroxide (H2O2), and hydroxyl free radical (HO) [28].

After entering the body, regardless of the routes to exposure, nanoparticles are transported through the central circulatory system to various organs and tissues, including the liver, spleen, heart, kidneys and brain [29]**.** Magnesium has been recognized as a cofactor for more than 300 enzymatic reactions [30], such as those responsible for regulating blood pressure and lipid peroxidation [31]. Mg2+ was found to reduce the production of free radicals by inhibiting NADPH oxidase, which could stimulate the production of reactive oxygen species [32]. Also, Magnesium ions are also essential to glutathione synthesis [33]. MgNPs is an important functional metal oxide that has been widely used in various fields. Due to their smaller size, nanomaterials have novel properties, which is different from others [34]. According to the study of Sushma et al, who stated that the biologically synthesized MgNPs exhibit good antioxidant activity [35].

5. CONCLUSIONS

Through the results, The MgNPs have a high efficiency in limiting the spread of the doxorubicine in healthy tissues and thus reducing its toxicity, especially on the liver. The good effects of MgNPs is shown by the improvement in enzymatic, hematological markers or through reducing the oxidative stress confirm the effectiveness of these compounds in protecting the body of patients from the side effects of doxorubicin in liver.

DECLARATION OF COMPETING INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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REFERENCES

1. Golemis EA, Scheet P, Beck TN, et al. Molecular mechanisms of the preventable causes of cancer in the United States. Genes Dev. 2018;32(13-14):868-902. doi:10.1101/gad.314849.118
2. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. CA Cancer J Clin. 2020 Jan;70(1):7-30. doi: 10.3322/caac.21590. Epub 2020 Jan 8. PMID: 31912902.
3. Lakomkin VL, Abramov AA, Lukoshkova EV, Prosvirnin AV, Kapelko VI. [Prevention of Diastolic Dysfunction Caused by Doxorubicin by Mitochondrial Antioxidant Plastomitin]. Kardiologiia. 2020 Aug;60(7):98-102. DOI: 10.18087/cardio.2020.7.n1157.
4. Y.S. Ibrahim, A. Akram, W.J. Rajab, M.M. Ahmed, M.A. Mahmood, Assessment of some Biochemical Parameters among Pleural Liquid and Serum during Platinum-based Chemotherapy against Ovarian Cancer. Res. J. Pharm. Technol. 15(2022) 5665-5671. https://doi:10.52711/0974-360X.2022.00955
5. W.G. Choi, D.K. Kim, Y. Shin, R. Park, Y. Y. Cho, J.Y. Lee, H.C. Kang, H. S. Lee, Liquid Chromatography–Tandem Mass Spectrometry for the Simultaneous Determination of Doxorubicin and its Metabolites Doxorubicinol, Doxorubicinone, Doxorubicinolone, and 7 Deoxydoxorubicinone in Mouse Plasma. Molecules. 25(2020) 1254. https://doi:10.3390/molecules25051254
6. J. Lei, H. Wang, D. Zhu, Y. Wan, L. Yin, Combined effects of avasimibe immunotherapy, doxorubicin chemotherapy, and metal–organic frameworks nanoparticles on breast cancer. J. Cell. Physiol. 235 (2019) 4814-4823. https://doi:10.1002/jcp.29358
7. P. Aruna, N.M. Gayathiri, Cardioprotective Activity of Telmisartan, Metformin and its Combination against Doxorubicin Induced Myocardial Infarction in Rat Model. Research J. Pharm. and Tech. 11(2018) 5293-5296. https://doi:10.5958/0974-360X.2018.00964.2
8. A. Allameh, R. Niayesh-Mehr, A. Aliarab, G. Sebastiani, K. Pantopoulos, Oxidative Stress in Liver Pathophysiology and Disease. Antioxidants, 12 (2023) 1653. https://doi.org/10.3390/antiox12091653
9. A.D. Mubarak, M.A.P. Manzoord, A. Sabarinathan, C.A. Devi, P.D. Rekha N. Thajuddin, S-Y. Lee, An investigation of antibiofilm and cytotoxic property of MgO nanoparticles. Biocatal. Agric. Biotechnol. 18(2019) 101069. https://doi:10.1016/j.bcab.2019.101069
10. W. Chartarrayawadee, P. Charoensin, J. Saenma, T. Rin, P. Khamai, P. Nasomjai, C.O. Too, Green synthesis and stabilization of silver nanoparticles using Lysimachia foenum-graecum Hance extract and their antibacterial activity. Green Process. Synth. 9(2020) 107-118. https://doi:10.1515/gps-2020-0012
11. R. Enobong, V.N. Essien, A.O. Atasie, D.O.N. Okeafor, Biogenic synthesis of magnesium oxide nanoparticles using Manihot esculenta (Crantz) leaf extract. Int. Nano Lett. 10(2019) 1-6. https://doi:10.1007/s40089-019-00290-w
12. L.P. Poka, K.G. Mohan, K.V. Rao, K. Shanker, Biosynthesis, characterization and acute oral toxicity studies of synthesized iron oxide nanoparticles using ethanolic extract of Centella asiatica plant. Mater. Lett. 236(2019) 256-259. https://doi:10.1016/j.matlet.2018.10.037
13. R. Prasanth, S. Dinesh Kumar, A. Jayalakshmi, G. Singaravelu, K. Govindaraju, V. Ganesh-Kumar, Green synthesis of magnesium oxide nanoparticles and their antibacterial activity. Indian J. Mar. Sci. 48(2019) 1210-1215.
14. A.A. Al Qahtani, A.M.M. Osman, Z.A. Damanhouri, H.M. Al-Kreathy, H.S. Al-Malky, W.S. Ramadan, F.O. Kamel, Cardioprotective Effect of Marine Astaxanthin on Doxorubicin-Induced Cardiotoxicity in Normal Rats. J. Pharm. Res. Int. 27(2019) 1-11. https://doi:10.9734/JPRI/2019/v27i330170
15. J. Sastre, F.V. Pallardó, J. García de la Asunción, J. Viña, Mitochondria, oxidative stress and aging. Free Radic. Res. 32(2000) 189-198 https://doi:10.1080/10715760000300201
16. G. Weckbecker, J.G. Cory, Ribonucleotide reductase activity and growth of glutathione-depleted mouse leukemia L1210 cells in vitro. Cancer Lett. 40(1988) 257-264. https://doi:10.1016/0304-3835(88)90084-5
17. C. Beauchamp, I. Fridovich, Superoxide dismutase: Improved assays and an assay applicable to acrylamide gels. Anal. Biochem. 44(1971) 276-287. https://doi:10.1016/0003-2697(71)90370-8
18. W.H. Habig, M.J. Pabst, W.B. Jakoby, Glutathione S-transferase. The first enzymatic step in mercapturic acid formation. J. Biol. Chem. 249(1974) 7130-7139.
19. J. Tariq, S. Shumaila, S. Riaz, S. Afzal, S. Hussain, S. Riaz, M. Uzair, B. A. Chaudhary, Phytochemical and Biological Evaluation of Ocimum basilicum Roots. Int J Pharm pharmaceut Res Hum. 2 (2016) 292-301.
20. M.M. Rahman, M.S. Rahaman, M.R. Islam, Role of Phenolic Compounds in Human Disease: Current Knowledge and Future Prospects. Molecules.

2021;27(1):233. Published 2021 Dec 30. doi:10.3390/molecules27010233

21. O. Solabomi, B. Ogunyemia, F. Zhanga, Y. Abdallaha, M. Zhanga, Y. Wangc, S. Guochang, W. Qiua, B. Li, Biosynthesis and characterization of magnesium oxide and manganese dioxide nanoparticles using Matricaria chamomilla L. extract and its inhibitory effect on Acidovorax oryzae strain RS-2. Artif. cells nanomed. biotechnol. 47(2019) 2230-2239. https://doi:10.1080/21691401.2019.1622552
22. M.M. Imani, M. Safaei, Optimized Synthesis of Magnesium Oxide Nanoparticles as Bactericidal Agents. J. Nanotechnol. 2019(2019) 1-6. https://doi:10.1155/2019/6063832
23. A. Yasmine, O. Solabomi-Olaitan, A. Amro, Z. Muchen, H. Xianxian, I. Ezzeldin, H. Afsana, F. Hatem, L. Bin, C. Jianping, The Green Synthesis of MgO Nano-Flowers Using Rosmarinus officinalis L. (Rosemary) and the Antibacterial Activities against Xanthomonas oryzae pv. oryzae. Biomed Res. Int. 2019(2019) 5620989. https://doi:10.1155/2019/5620989
24. J.N. Sushma, D. Prathyusha, G. Swathi, Facile approach to synthesize magnesium oxide nanoparticles by using Clitoria ternatea—characterization and in vitro antioxidant studies. Appl. Nanosci. 6(2016) 437- 444. https://doi:10.1007/s13204-015-0455-1
25. I. Boulaares, I.Y. Guemari, S. Derouiche, Analysis of Some Hematological and Biochemical Markers in Women Cancer Patients Receiving Doxorubicine Chemotherapy. J. Pharm. Biosci. 8(2020) 29-34. https://doi:10.20510/ukjpb/8/i1/1581327899
26. M.H. Shaty, M.I. Al-Ezzi, I.S. Arif, D. Basil, Effect of Metformin on inflammatory markers involved in Cardiotoxicity induced by Doxorubicin. Res. J. Pharm. Technol. 12(2019) 5815-5821. https://doi:10.5958/0974-360X.2019.01007.2
27. A. Gasser, Y.W. Chen, A. Audebrand, A. Daglayan, M. Charavin, B. Escoubet, C.G. Nebigil, Prokineticin Receptor-1 Signaling Inhibits Dose- and Time-Dependent Anthracycline-Induced Cardiovascular Toxicity Via Myocardial and Vascular Protection. J.A.C.C.: Cardio Oncology. 1(2019) 84-102. https://doi:10.1016/j.jaccao.2019.06.003
28. A. Hajare Ashok, A. Powar Trupti, M. Bhatia Neela, N. More Harinath, Development and Validation of RP-HPLC Method for Determination of Doxorubicin Hydrochloride from Vacuum Foam Dried Formulation. Res. J. Pharm. Technol. 9(2016) 1352-1356. https://doi:10.5958/0974-360X.2016.00259.6
29. A. Staroń, O. Długosz, J. Pulit-Prociak, M. Banach, Analysis of the Exposure of Organisms to the Action of Nanomaterials. Materials. 13(2020), 1-18. https://doi:10.3390/ma13020349
30. U. Gröber, J. Schmidt, K. Kisters, Magnesium in Prevention and Therapy. Nutrients. 7(2015) 8199-8226. https://doi:10.3390/nu7095388
31. J.J. DiNicolantonio, J. Liu, J.H. O'Keefe, (2018). Magnesium for the prevention and treatment of cardiovascular disease. Open Heart. 5(2018) e000775. https://doi:10.1136/ openhrt-2018-000775
32. C.-x. Zhang, F. Huang, J. Li, L. Wang, K. Song, K.-s. Mai, Interactive effects of dietary magnesium and vitamin E on growth performance, body composition, blood parameters and antioxidant status in Japanese seabass (Lateolabrax japonicus) fed oxidized oil. Aquac. Nutr.22 (2016) 708-722 https://doi:10.1111/anu.12393
33. K. Pasternak, J. Kocot, A. Horecka, Biochemistry ofmagnesium. J. Elem. 15(2010), 601-616. https://doi:10.5601/jelem.2010.15.3.601-616
34. S. Narendhran, S.A. Sabana, R. Vishnu, Cytotoxic Activity of Green And Chemically Synthesized Magnesium Oxide Nanoparticles Against Siha Cell Line. Int. J. Life Sci. Res. (2019) 43-47.
35. J.N. Sushma, D. Prathyusha, G. Swathi, T. Madhavi, B. Deva Prasad Raju, K. Mallikarjuna, H.S. Kim, Facile approach to synthesize magnesium oxide nanoparticles by using Clitoria ternatea—characterization and in vitro antioxidant studies. Appl. Nanosci. 6(2015) 437-444 https://doi:10.1007/s13204-015-0455-