Toxoplasmosis is a cosmopolitan parasitic disease that impacts enormous population sector. In this work we investigated the antitoxoplasmic therapeutic effect of one synthetic drug; nitazoxanide (NTZ) and another agent of plant origin; *Zingiber officinale* (ginger) as adjuvant to the traditional antitoxoplasmic drugs (pyrimethamine & sulphadiazine) on experimental murine toxoplasmosis (RH virulent strain). Animals were classified into 7 groups; GI: Non-infected, non-treated (normal control), GII: Infected non-treated mice (infected control), GIII: Infected & treated by a combination of pyrimethamine & sulphadiazine (drug control), Group IV: Infected & treated by *Zingiber officinale* (ginger) as adjuvant to the traditional antitoxoplasmic drugs, Group V: Infected & treated by nitazoxanide, GVI: Infected & treated by combination of *Zingiber officinale* and pyrimethamine & sulphadiazine, Group VII: Infected & treated by combination of *Zingiber officinale* & nitazoxanide. For assessment of the therapeutic effect of various drug regimens on acute toxoplasmosis, survival rate and intraperitoneal fluid tachyzoite count were calculated. In the present study, Group VI achieved the best results among all studied groups so as to the survival rate increased to 70% and the tachyzoites count reduction rate was up to 72.9% as compared with the infected control mice. Inversely, group IV results were the lowest all over other groups with 20% survival and 33.3% tachyzoite reduction rates respectively. In between, the other groups lied in the grey zone and their corresponding measurements were as following: Group III, Group V and Group VII achieved 60%, 70%; 50, 58% and 40%, 55.5% for survival and tachyzoite reduction rates respectively. These results denote that nitazoxanide could be an acceptable, standardized, characterized, already FDA approved and commercially available substitute to traditional antitoxoplasmic synthetic drug. Also *Zingiber officinale* would be a safe and beneficial adjuvant treatment that potentiates the antitoxoplasmic action.
of the traditional treatment of toxoplasmosis. More studies are needed to address the dose response relationship of both NTZ and *Zingiber officinale* before using them for treatment of acute toxoplasmosis.

**INTRODUCTION**

More than one billion people worldwide are anticipated to harbor *Toxoplasma gondii* (*T.gondii*) infection frequently with many lifelong health consequences. Toxoplasmosis is a significant cause of food borne, inflammatory diseases, as well as congenital malformations (Oz, 2014). In Egypt a study by (Kamal et al., 2015) stated that the *T. gondii* infection seroprevalence among the high risk pregnancy group was 50.8% versus 8.3% among the normal pregnant women. Toxoplasmosis is implicated in post-delivery adverse pregnancy outcomes at a ratio of 80.3% and abortion was the highest detected complication. Ocular toxoplasmosis is a vision-threatening disease and toxoplasmic retinochoroiditis is the most widespread cause of posterior uveitis in immunocompetent patients (Dukaczewska et al., 2015) Besides, toxoplasmosis is deadly in the immunocompromised individuals such as cancer patients under chemotherapy (Jiang et al., 2015). Presently used therapies are ineffective for persistent chronic disease and congenital toxoplasmosis or have severe side effects which may result in life-threatening complications. There is a pressing need for safe and effective therapies to treat this broad-based contagious and inflammatory disease (Oz, 2014). Spiramycin monotherapy has been used for prophylaxis and treatment of fetomaternal toxoplasmosis. Spiramycin monotherapy is effective in early pregnancy as a preventive measure but not after fetal exposure to the infection. In a prospective cohort trial in Brazil 58% of newborns from spiramycin-treated women, in contrast to over 73% from untreated ones had congenital infection (Avelino et al., 2014). The combination of pyrimethamine and sulphadiazine remains the mainstay for treatment and prophylaxis of the majority of clinical presentations of toxoplasmosis. However, this therapeutic regimen is not always suitable for lengthened treatment because of emergence of undesirable side effects and it may contribute to clinical failure by electing drug-resistant parasite strains. Consequently, new therapies are vitally needed (Reich &Mackensen, 2015). There is a mounting alertness of the therapeutic potential of natural products and medicinal herbs that are habitually believed to be less toxic and seem free from side effects than synthetic drugs, particularly in pregnant women where the administration of empiric antimicrobial therapy is unsafe measurement. (Hökelek and Bronze, 2015). Many herbal plants extracts exhibit anti-*Toxoplasma* activity including *Myrrh* (AL-Zanbagi, 2007), *Piper nigrum*, *Capsicum frutescens*, *Curcuma longa* (AL-Zanbagi, 2009), *Nigella sativa* (Rayan et al., 2011). Ginger (*Zingiber officinale*) belongs to *Zingiberaceae* family, it is one of the famous spices globally. It has been used for curing menstruation disorder, cardiac problems, food poisoning, osteoarthritis, cough, nausea, inflammation, motion sickness, epilepsy, cold, menstrual cramps, cancer and many more. Additionally, it also exhibits antimicrobial and antioxidant properties. Medicinal value of ginger and its knowledge supply researchers by a good platform for pro-
spect research studies aiming for protection of human population from several diseases categories (Gupta and Sharma, 2014). Also ginger is an helpful non pharmacological management of nausea and vomiting during early pregnancy (Thomson et al., 2014). Ginger is used in parasitology area for treatment of *Giardia lamblia* (Mahmoud et al., 2014), *Anisakis simplex* (Lin et al., 2010), *Echinococcus granulosus* (Baquer et al., 2014), *Schistosoma mansoni* (Mostafa et al., 2011; Hassan et al., 2016), *H. nana* (Lin et al., 2014) and *blastocystis* (Abdel-Hafeez et al., 2015). Nitazoxanide, 2-acetyloxy-N-(5-nitro-2-thiazolyl) benzamide is a new nitrothiazolebenzamide compound distinguished for its activity in treating both intestinal helminthic and protozoal infections, besides, it is used as a first line treatment for *cryptosporidiosis* (Ali et al., 2014). Galván-Ramírez et al. (2013) reported that nitazoxanide reduced *T. gondii* infection in vitro more than pyrimethamine and found to be not cytotoxic to astrocytes at the administered dose. This *invivo* study aimed to explore the possible efficacy of ginger as combined with classical drugs and nitazoxanide treatment against *T. gondii* acute infection as a step on the way to create a potential synthetic and herbal candidates for effective and safe treatment of toxoplasmosis.

**MATERIALS AND METHODS**

This study was conducted in NRC-zoonotic diseases department. The animal experiment was carried out according to the internationally valid guidelines and the research protocol was approved by Research Ethics Committee, Faculty of Medicine, Benha University, Egypt.

I. Parasite

The RH virulent strain of *T. gondii* was maintained by routine intraperitoneal passage every 72 hours after they were obtained from NRC. The tachyzoites concentration was determined by means of a haemocytometer. It was re-suspended at a density of $2 \times 10^7$/ml in saline to be inoculated intraperitoneally into the mice (Grujić et al., 2005).

II. Experimental animals:

A total of 95 laboratory-bred male Swiss albino mice, 10 weeks-old, weighing ~ 30g, were selected from the animal house of NRC. They were housed in plastic cages (5 mice/cage) with white wood chips for bedding, fed by commercial complete food mixture and tap water for drinking and maintained under controlled conditions of lighting (12 h light/12 h dark cycle) and temperature (25±2°C).

III. Drugs and Plant Materials:

**Sulfadiazine and pyrimethamine:**

_Sulfadiazine:_ (Dohms Laboratories) and pyrimethamine (Sigma Chemical Co., St.Louis, Mo.), were provided in powder form and prepared daily as liquid suspensions; after brief sonication, the homogenized suspensions were administered orally to mice via tube feeding.

**Nitazoxanide:**

Nitazoxanide was available as tablets and suspension forms. In this study the suspension form (100mg/5ml) produced by Medizen Pharmaceutical Industries for Utopia Pharmaceuticals was used. Each 5ml suspension contains:

<table>
<thead>
<tr>
<th>Active Ingredients: Nitazoxanide 100mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inactive Ingredients: Sucrose, pregelati-</td>
</tr>
</tbody>
</table>
nized starch, carboxy methyl cellulose sodium, FD & C red citric acid, acacia gum, microcrystalline cellulose, xanthan gum, sodium benzoate and strawberry flavor.

Ginger:

Ginger was available as tablets stored at temperature not exceeding 30°C, each tablet contained 400mg ginger extract (Zingiber Officinale). The tablets were crushed and dissolved in distilled water. The form used in this study was a product of Arab Co. for Pharmaceuticals and Medicinal Plants “MEPACOMEDIFOOD”, Egypt.

IV. Experimental infection:

Mice were injected intraperitoneally with $2 \times 10^2$ tachyzoites of T. gondii RH strain and assigned to treatment (Grujić et al., 2005 and AL-Zanbagi, 2009).

V. Experimental Design

Animals were classified into 7 groups (15 each) except normal control (5 mice), with 5 mice per group allocated to scarifying and tachyzoite counting and the rest were left for observing survival rate; Group I: Non-infected, non-treated (normal control) and received 0.1 ml of sterile distilled water. Group II: Infected non-treated mice (infected control). Group III: Infected and treated by pyrimethamine (12.5 mg/kg/day) and sulphadiazine at a dose of 200 mg/kg/day. (Romand et al. 1993). Group IV: Infected and treated by Zingiber Officinale; 500mg/kg (Hassan et al., 2016). Group V: Infected and treated by nitazoxanide; 200mg/kg. (El-Taweel et al.,2016). Group VI: Infected and treated by combination of Zingiber Officinale (150mg/kg) (Sanderson et al., 2002) + pyrimethamine and sulphadiazine treatments in the same previous doses. Group VII: Infected and treated by combination of Zingiber Officinale (150mg/kg) (Sanderson et al., 2002) and nitazoxanide 100mg/kg (Li et al., 2003). For all treated groups, treatments were started 24 hours post infection and administered daily at a fixed hour for 15 days.

VI. Assessment of anti-Toxoplasma effects of studied drugs:

The survival rate in all groups were reported till 3rd week in 65 mice and the peritoneal fluids of the 30 mice were examined on the 8th day (Grujić et al., 2005). The number of tachyzoites was counted with a hemocytometer, fixed and stained with trypan blue, examined by light microscope at x100 magnifica-

![Fig. (1): T = tachyzoites](image)
tion as seen below and compared with the infected control groups.

3. Statistical analysis.

The data were recorded on a report form, tabulated and analyzed using SPSS (Statistical package for social science) version 20. ANOVA test was used to compare the means of more than 2 groups. Post hoc test (Bonferroni) for pairwise group comparison was used to assess inter-group difference between each 2 groups. Chi-square was used to assess the statistical significance between various groups survival rates. The tachyzoite reduction rates were assessed using the formula: (Mean value of the infected untreated group - mean value of infected- treated group) X 100 / Mean value of infected- untreated group (Abdel Salam et al., 2008). A P value <0.05 was considered statistically significant (*) while >0.05 statistically insignificant P value <0.01 was considered highly significant (**) in all analyses.

RESULTS

In Table 1: All groups showed a statistically significant lower survival rate than normal control group except G VI treated by combination of pyrimethamine and sulfadiazine +ginger, which showed an insignificant difference regarding survival rate than normal control group, implying the excellent antitoxoplasmic effect of this drug combination being kept the mice lives as efficient as if they were not infected. There was a borderline significant difference in survival rate between infected control group and group VI denoting a relatively higher response of this treatment regimen than other groups including drug control group treated by pyrimethamine and sulfadiazine (G III) as they all showed insignificant difference with infected control group survival rate. There was no significant difference between drug control group and all other groups survival rates as compared individually by the former, which indicates an observable efficacy of those groups tested drugs (Table 1, Figure 2).

In table 2, a statistically significant difference between the studied groups mean tachyzoite counts (F=29.341, p value <0.001), was found which points to the considerable variations between them as regard their activity against acute Toxoplasma infection. To assess the probable significant difference between each two groups, Post hoc test (Bonferroni) for pairwise multiple comparison was run between groups which revealed that the difference in the mean tachyzoite count was:

A significant statistical difference when comparing between infected control group and all groups, that indicates an observable efficacy of all tested drug regimens (emphasized the impression taken as a result of table 1 data analysis).

An insignificant statistical difference when comparing between drug control group III (treated by combination of pyrimethamine and sulfadiazine) and all other groups except group VI, which emphasized the considerable antitoxoplasmic effect of all studied drug regimens as mentioned above and the worthy note superiority of group VI (treated by combination of pyrimethamine and sulfadiazine +ginger), which showed a lower tachyzoite mean than the drug control one, denoting an excellent response to this treatment regimen.
• A significant statistical difference when comparing ginger group (IV) and all other groups except group VII (treated by Nitazoxanide + Ginger), its tachyzoite count was higher than all groups except infected control group.

• A significant statistical difference when comparing between group V (Nitazoxanide treated) and that of infected control group (II) and group VI (ginger). Its mean tachyzoite count was lower than that of group II, IV and VII while higher than that of group III and VI.

• A significant statistical difference when comparing between group VI (Pyrimethamine & sulfadiazine + Ginger) and that of infected control group (II) and ginger group (IV) only. Its mean tachyzoite count was the lowest among all studied groups.

• A significant statistical difference when comparing between group VII (NTZ + Ginger) and that of infected control group (II) only. Its mean tachyzoite count was lower than that of infected control group (II) and ginger (IV), while it was higher than that of III, V and IV groups.

Group VI (Pyrimethamine & sulfadiazine + Ginger) achieved the best tachyzoite reduction rate among all studied groups (72.9%). The other groups tachyzoite reduction rates were: 70%, 33.3%, 58% and 55.5% for groups III, IV, V, and VII respectively (Figure 3). Generally there was an observable harmony between survival rates and tachyzoite reduction rates of all groups as shown in Figure 4.

![Mice survival rate after 3w.](image)

Figure (2): Mice survival rates after different drug regimens at the 3rd week post infection in acute toxoplasmosis.
Table (1): Mice survival rate after different treatment regimens as compared with those of normal control, infected control and drug control groups during various experimental time points.

<table>
<thead>
<tr>
<th>Animal group</th>
<th>Survival rate after 1w</th>
<th>Survival rate after 2w</th>
<th>Survival rate after 3w</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Original No</td>
<td>%</td>
<td>No</td>
</tr>
<tr>
<td>Normal control (I)</td>
<td>5 100 5 100</td>
<td>-</td>
<td>10 100 4 40</td>
</tr>
<tr>
<td>Infected control (II)</td>
<td>10 100 4 40</td>
<td>2 20</td>
<td>10 100 9 90</td>
</tr>
<tr>
<td>Pyrimethamine &amp; sulfa diazine (III)</td>
<td>10 100 9 90</td>
<td>6 60</td>
<td>10 100 9 90</td>
</tr>
<tr>
<td>Ginger (IV)</td>
<td>10 100 9 90</td>
<td>7 70</td>
<td>10 100 9 90</td>
</tr>
<tr>
<td>Nitazoxanide (V)</td>
<td>10 100 9 90</td>
<td>4 40</td>
<td>10 100 9 90</td>
</tr>
<tr>
<td>Pyrimethamine &amp; sulfa diazine + Ginger (VI)</td>
<td>10 100 9 90</td>
<td>7 70</td>
<td>10 100 9 90</td>
</tr>
<tr>
<td>Nitazoxanide + Ginger (VII)</td>
<td>10 100 9 90</td>
<td>4 40</td>
<td>10 100 9 90</td>
</tr>
</tbody>
</table>

* significant  ** highly significant

Acute Toxoplasmosis

Table (2): Analysis of variance in the mean tachyzoite count after different treatment regimens.

<table>
<thead>
<tr>
<th>Animal group</th>
<th>Total</th>
<th>Mean no. of tachyzoites</th>
<th>Pairwise Group Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infected control(II) /b</td>
<td>5</td>
<td>4651.0</td>
<td>991.7</td>
</tr>
<tr>
<td>Pyrimethamine &amp; sulfa diazine (III) c</td>
<td>5</td>
<td>1392.0</td>
<td>210.5</td>
</tr>
<tr>
<td>Ginger (IV) d</td>
<td>5</td>
<td>3100.0</td>
<td>435.9</td>
</tr>
<tr>
<td>Nitazoxanide (V) e</td>
<td>5</td>
<td>1952.0</td>
<td>400.6</td>
</tr>
<tr>
<td>Pyrimethamine &amp; sulfa diazine + Ginger (VI) f</td>
<td>5</td>
<td>1260.0</td>
<td>194.9</td>
</tr>
<tr>
<td>Nitazoxanide + Ginger (VII) g</td>
<td>5</td>
<td>2070.0</td>
<td>521.5</td>
</tr>
</tbody>
</table>

* significant  ** highly significant
b: significant when compared with infected control group (II) c: significant when compared with drug control group (III) d: significant when compared with ginger group (IV) e: significance when compared with NTZ group (V) f: significant when compared with Pyrimethamine & sulfa diazine + Ginger group (VI) g: significant when compared with Nitazoxanide + Ginger group (VII)
Figure (3): The mean tachyzoite reduction rate after different treatment regimens of acute toxoplasmosis.

Figure (4): Relation between the mice survival rates and the corresponding tachyzoite reduction rates after various treatment regimens.
DISCUSSION

The treatment of *T. gondii* infection emphasizes the problematic issue of the inadequate effectiveness of the existing antiparasitic agents and their side effects and also, the possible appearance of resistant *Toxoplasma* strains (EL-Sayed and Safar, 2014). Discovery of low toxicity compounds and competent to prevent and treat *T. gondii* would be extremely beneficial for treatment of infections in immunocompromised patients (Gomes et al., 2012). The medicinal herbs value as sources of natural product bioactive molecules to medicine is ascribed to not only in their pharmacological or chemotherapeutic outcome, but also in their role as parent molecules for the manufacture of new drug substances (EL-Sayed and Safar, 2014). The rhizomes of the ginger (*Zingiber officinale*) are regularly used as a flavor or food supplement. There are some antioxidants and anti-inflammatory constituents in ginger rhizomes (Ahui et al., 2008 & Haniadka et al., 2013). In the parasitological field, previous studies have confirmed that ginger and its constituents have significant nematocidal, cestocidal and anti-protozoal activities *in vitro* and *in vivo* (El-Sayed and El-Saka, 2015). Nitazoxanide is a broad-spectrum anti-parasitic and broad-spectrum antiviral drug that is indicated in medicine for the management of diverse helminthic, protozoal and viral infections (Di Santo and Ehrisman, 2013 and Rossignol et al., 2014). In this study we assessed the therapeutic antitoxoplasmic effect of both ginger which was mentioned before to have antitoxoplasmic activity in some handful studies (Choi et al., 2008 and Choi et al., 2013) and nitazoxanide which was reported before to have an *in vitro* antitoxoplasmic activity (Galván-Ramírez et al., 2013), but up to our knowledge, no *in vivo* studies checked its antitoxoplasmic properties yet. Including the traditional mainstay antitoxoplasmic treatment (pyrimethamine and sulphadiazine), we designed versatile drug regimens to explore the synergistic and/or antagonistic activities of newly studied drugs as mentioned in material and methods section. In the present work, group VI (treated by combination of, pyrimethamine and sulphadiazine + *Zingiber officinale*) accomplished the best therapeutic efficacy among studied groups as with this treatment regimen survival and tachyzoites reduction rates were 70% and 72.9% respectively. Inversely was the ginger treated group (group IV) which showed the lowest results among all groups with 20% and 33.3% for survival and tachyzoites reduction rates respectively. In-between, other groups lied in the grey area with the best performance within those medium acting drug regimens for group III, treated by pyrimethamine and sulphadiazine (drug control group), it achieved 60% and 70% for survival and tachyzoites reduction rates respectively. In nitazoxanide treated mice, the corresponding rates were 50% and 58% orderly. These rates were surprisingly diminished upon adding ginger as adjuvant to nitazoxanide treatment to reach 40%, 55.5% for survival and tachyzoites reduction rates, which may be related to using a smaller dose of NTZ (100mg/kg) in this regimen. (Tables 1, 2 & Figures 2-4). Analyzing the variance between the mean tachyzoite count of various studied groups, it was observed that groups III, V and IV were identical regarding their performance as antitoxoplasmic agents.
when compared with all other groups; they all showed a statistically significant difference against the same groups (II & IV), denoting that both newly studied regimens in this study (V and IV) have proved a comparable efficiency in toxoplasmosis treatment as good as the drug control currently used in treatment of toxoplasmosis (group III) (Table 2). In this study, ginger exhibited some activity against *T. gondii* in experimentally infected mice when used alone in 500mg/kg per mice as compared by infected control group, this antitoxoplasmonic activity was formerly reported by Choi et al. (2013) who evaluated the anti-parasitic effect of GEF1 (fraction 1 obtained from ginger extract) against *T. gondii* in vitro and in vivo. They demonstrated that GEF1 not only triggers anti-*T. gondii* effects leading to the inactivation of apoptotic proteins in infected host cells by direct inhibition of *T. gondii* but also possesses anti-parasitic properties which hinder inflammatory cytokine secretion in vivo so as to the parasite activity was strongly affected after GEF1 treatment, the anti-inflammatory properties of ginger mentioned by them were also reported before by Kuo et al. (2011), Wang et al. (2011), Ha et al. (2012) and Ajayi et al. (2015), which may explain the performance superiority that tinged the results of group VI which was treated by combination of and pyrimethamine & sulfadiazine, and ginger as we can hypothesize that the potentiating antitoxoplasmic action exerted by ginger to pyrimethamine & sulfadiazine may be due to those anti-inflammatory properties. Also, the direct antiparasitic inhibitory action mentioned before by Choi et al. (2013) could be the leading cause of the observed decrease in tachyzoite number like what happens with the classical anti *Toxoplasma* drugs which when started promptly after infection, caused rapid resolution of retinochoroiditis lesions, prevented wide spread tissue destruction, decreased the chances of the parasite dissemination and reduced lesion size and vitreal inflammation as well as improved visual acuity. (Soheilian et al., 2011). The antioxidant effect of ginger reported previously by Verma and Asnani. (2007), Sakr, (2007) and Mostafa et al. (2011) might also be a potential cause for its antitoxoplastic effect in this study. However, in this study, using ginger alone even in its high dose didn’t give a satisfactory effect on the parasite yield so as to a statistically significant difference was found between the tachyzoite count of ginger treated group and all other groups except group VII, so much like the results of infected non treated control group (group II) (Table 2), the difference between our results of ginger treated group from that reported by Choi et al. (2013) could be understood in view of knowing that their results about ginger antitoxoplasmic activity were verified by using GEF1 (fraction 1 obtained from ginger extract) which may have different pharmacological properties than the whole herb extract used in this experiment. Concerning nitazoxanide results, they were in contrast with those of Galván-Ramírez et al. (2013) who said that nitazoxanide decreased *T. gondii* infection in vitro more than pyrimethamine and was not cytotoxic to astrocytes at the administered dose. This controversy could be explained by that they evaluated the nitazoxinide efficacy in an in vitro experiment while ours was in vivo one, where several host metabolic factors may im-
pact the drug yield, additionally the drug’s own pharmacokinetics; absorption, degradation to active metabolites with different activity, excretion and bioavailability surely influences the therapeutic action which is not the case in in vitro studies in which only the parent drug is tested with elimination of the possible effect of all other in vivo study mentioned factors. However, the overall efficacy rates of NTZ as antitoxoplastic agent was so close to what has been reported in other in vivo studies against Cryptosporidium parasites in which treatment with NTZ as a powder or as an injectable formulation administered orally yielded only moderate efficacy: 42 or 26% of the oocyst output in controls, respectively, (Blagburn et al., 1998). The NTZ possible effective mechanism of action might be attributed to being a noncompetitive inhibitor of the pyruvate: ferredoxin/flavodoxin oxidoreductases (PFORs) which catalyze the oxidative decarboxylation of pyruvate to acetyl coenzyme A (acetyl-CoA) and CO₂, with reducing equivalents transferred to either ferredoxin or flavodoxin. These enzymes are present in the amitochondriate eukaryotic human protozoa; Trichomonas vaginalis, Entamoeba histolytica, and Giardia intestinalis, Cryptosporidium parvum (Hoffman et al., 2007) and Toxoplasma apicoplast, where it operates as a general electron switch at the bifurcation step of many different electron transfer pathways (Singh and Bhakuni, 2008). Consequently, NTZ using this mechanism, might hinder the crucial parasitic respiratory processes leading to their death and diminishing invasion of new host cells thus alleviating the parasitic yield for the sake of affected host tissues. Another valuable fact that favors using NTZ as antitoxoplasmic agent is being better as regard safe use during pregnancy as it is classified by FDA as B category which means that animal studies show no risks, but there are no controlled studies on pregnant women are available, so it is considered safe to use if there is clinical need during (Product Information. Alinia [nitazoxanide], 2005), while the traditional anti Toxoplasma treatment (pyrimethamine & sulfadiazine) are classified by FDA as C category, which means that animal studies have shown risk to the fetus and there are no controlled studies in women (CDC report, 1997). Since the main toxoplasmic health hazards are happening due to feto-maternal transmission, so availability of new drug with better safety during pregnancy and having comparable therapeutic antitoxoplasmic effect is believed to be considerably valuable for prevention or reducing the risk of Toxoplasma feto-maternal transmission. In conclusion, this study demonstrated the excellent efficacy of both nitazoxanide monotherapy and Zingiber officinale + pyrimethamine and sulfadiazine triple therapy in treatment of acute toxoplasmosis. Further studies are recommended in order to investigate the effectiveness of various dose response relationship of NTZ regimens against T. gondii on a wider experimental scale. Fortunately, it is FDA approved, categorized as safer than currently used drugs during pregnancy, and already globally marketed, this will too much facilitates starting clinical trials to assess repurposing it against toxoplasmosis. Also, introduction of ginger as a routine food supplement during treatment of acute toxoplasmosis could safely offer more efficacy.
to the currently used traditional antitoxicoplamic drugs.

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Conflict of interest The authors declare that they have no conflict of interest. Human and animal rights informed consent. This study was approved by the Scientific Research Ethical Committee, Faculty of Medicine, Benha University. The experimental animal studies were conducted in accordance with international guidelines for animal care. All experimental mice were housed under standard laboratory conditions with an average temperature of 20–25 °C and were given drinking water and regular mouse diet.

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دراسة التأثير العلاجي لعشب الزنجيبيل وعقار النيتازوكسانيد على الفئران المصابية بداء المقوسات (التوكسوبلازما) الحادة

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قسم الطفيليات الطبية-كلية الطب البشري-جامعة بنها١
قسم الأمراض المشتركة- المركز القومي للبحوث

داء المقوسات هو مرض طفيلي عالمي يؤثر على قطاع هائل من السكان. في هذا العمل، نقيم التأثير العلاجي لدواء النيتازوكسانيد وأخر من أصل نباتي (الزنجبيل) على الفئران المصابية بداء المقوسات التجريبية (السلالة الفتاكة) مقزنة بالأدوية التقليدية المستخدمة حاليا في علاج داء المقوسات للإنسان (بيريميثيامين والسلافاديازين). تم تصنيف الحيوانات إلى 7 مجموعات، المجموعة الأولى: الفئران المصابية الغير المعالجة المجموعة الثانية: الفئران المصابية الغير معالجة، المجموعة الثالثة: الفئران المصابية، المجموعة الرابعة: الفئران مصحوبة بعلاج بالزنجبيل، المجموعة الخامسة: الفئران المصابية وعلاجها بوبريميثيامين والسلافاديازين، المجموعة السادسة: الفئران المصابية وعلاجها بمزيج من الزنجيبيل وبريميثيامين سلافاديازين، المجموعة السابعة: الفئران مصحوبة بعلاج بمزيج من الزنجيبيل وبريميثيامين السلافاديازين لتقييم فعالية الأدوية التي تم اختبارها. تم حساب معدل البقاء على قيد الحياة عند التاكوزيت داخل السائل البريتيوني. في هذه الدراسة، حققت المجموعة السادسة أفضل النتائج من بين مجموعات الدراسة وذلك لأنها زاد معدل البقاء على قيد الحياة إلى 70%، وانخفض معدل عدد التاكوزيت بنسبة 27.9%، وثبتت قياسات المجموعات الأخرى جميعها تقل عن المجموعة السادسة على النحو التالي: المجموعة الثالثة: 60%، المجموعة الرابعة: 20%، المجموعة الخامسة: 55%، وأخيرا المجموعة السابعة: 60% و55% للبقاء على قيد الحياة وتختلف معدل عدد التاكوزيت داخل السائل البريتيوني على الترتيب. هذا يدل على أن

Acute Toxoplasmosis

دواء النيتازوكسانيد يمكن أن يكون عقاراً يقبل ضد داء المقوسات الحادة كما أن الزنجبيلا يمكن أن يكون علاج معاون جيد وآمن ضد داء المقوسات الحادة إذا تمت إضافته للأدوية التقليدية المستخدمة في علاجها. ما زالت هناك حاجة لمزيد من الدراسات على نطاق أوسع لتحديد العلاقة بين الجرعات المختلفة لعقار الزنجبيلا واستجابة مرضى التوكسولازما المحاذة للعلاج بهما.