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ORIGINAL ARTICLE

Synergistic Efficacy Study of Praziquantel and Ginger Alcoholic Extract as Antiparasitic in Vitro

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ABSTRACT

Background*: Hydatid disease is a disease caused by the tapeworm Echinococcus, and the parasite can infect the liver, lungs, etc. This disease poses a health risk due to the serious complications that may occur from it.* ***Objectives****: The present study aimed to know the effect of each of: praziquantel, ginger alcoholic extract, in addition to niosome loaded with ginger extract, as well as the synergistic complex of praziquantel with niosome loaded with ginger extract, in eliminating the protoscolices of hydatid cysts in vitro.* ***Metheology****: After Preparation of alcoholic ginger extract and noisome loaded with it, the effects of different therapeutic compounds on the protoscole were tested using concentrations (5, 10, 20, 30, 50, 100, 150 mg/ml) of each extract, with incubation periods ranging from 5 to 60 minutes.* ***Results****: The results for the synergistic compound loaded with niosomal extract and ginger extract produced the highest extermination rate of 79% after 60 minutes. While, praziquantel extermination rate ranged from 66% to 79% and ginger extract at 5 mg/ml showed extermination ranging from 32% to 40%. Statistical tests reveal significant differences between treatments with ANOVA test results ($F=11$; $p<0.00018$) showing the high efficacy of the synergistic compound over praziquantel and ginger extract.* ***Conclusion****: The synergistic combination of niosome loaded with ginger extract and praziquantel showed high efficacy in vitro protoscolices extermination rates, but the standard deviation value of data analysis confirmed the presence of a state of instability. Niosome loaded with ginger extract showed excellent extermination efficacy with stable effects. Therefore, it is considered the best choice as a treatment. The extermination efficacy of praziquantel and ginger alcoholic extract was within the average values.*

INTRODUCTION

Hydatid disease is a chronic infection of humans that occurs worldwide. It occurs when the eggs of the nematode Echinococcus granulosus enter the body.[1] Symptoms are delayed, taking months or even years to become noticeable, making early diagnosis a challenge. By the time infection is detected, hydatid cysts have often already formed in the body, and may have parasitized, grown, and increased in size, with the possibility of an increase in the number of cysts.[2] The hydatid cyst is the larval stage of the nematode Echinococcus granulosus. Studies indicate that 50-70% of hydatid cysts occur in the liver, while less commonly they occur in the lung, spleen, kidney, and occasionally in the bones and brain. In recent years, rare cases of hydatid cysts have been reported in uncommon locations.[2,3] The parasite's adaptation to grow in new tissues serves as a survival strategy, as it helps it evade the body's immune response.

Recently, confirmed cases of hydatid cysts have been reported in the tissues of the neck[4], and also in the eye tissues, which is a rare case.[5,6] Furthermore, cases of hydatid cysts in the central nervous system, including the spinal cord, have been confirmed in rare cases that have been diagnosed recently.[7] In this context, the boom of hydatid cysts in tissues that were formerly not able to conform to them appears to be proof of a huge evolution of the parasite. Given the resistance of the parasite to remedy, this imposes on researchers they want to broaden opportunity drugs that are extra effective and feature fewer side effects on patients. This is of paramount significance to reduce the unfold of this ailment, which has end up a monetary and social burden on society.

In view of those foremost challenges, there may be an urgent want for in addition studies and research geared toward enhancing the presently used treatments, in addition to developing new remedy alternatives. Therapeutic processes used to fight this disorder vary among surgical excision, the use of the Bayer aspiration approach, similarly to cautious observation and waiting inside the case of small cysts. Chemotherapy is likewise used in cases wherein there are a large wide variety of cysts in one organ or the unfold of cysts to more than one organ inside the body[1,2].

Medicinal plants still play a major role in the treatment of many diseases. One of the most prominent examples of this is ginger, which has gained wide fame in the field of preventive and therapeutic treatments. Research has shown many therapeutic properties of ginger extract, as its effectiveness as an antibiotic, antimicrobial, and antioxidant has been identified, in addition to its ability to inhibit the formation of inflammatory compounds, and other defensive and inhibitory mechanisms. Some studies have indicated the efficiency of ginger extract in combating the initial heads of the worm Echinococcus granulosus, which causes hydatid cysts. Despite the multiplicity of therapeutic compounds available, a scientific gap calls for the need to develop drugs continuously. Recent developments in the pharmaceutical industry, especially in the field of nano applications, contribute to improving the properties of therapeutic compounds and their means of release and loading, which enhances the effectiveness of drugs and contributes to the development of treatments significantly[8,9].

The current research focuses on comparing the therapeutic efficacy of each of the ethanolic extract of ginger on the viability of protoscolices in the laboratory, the drug praziquantel, niosomes loaded with ginger extract, as well as the efficacy of the synergistic compound consisting of combining the drug praziquantel with niosomes loaded with ginger extract, at different concentrations and for specific time periods in laboratory conditions. The research also includes evaluating the half-toxic dose of the studied compounds, in addition to studying the effect of these compounds on the process of cell apoptosis in protoscolices.

METHODOLOGY

Materials:

Collection of hydatid cysts

Hydatid cysts were collected from Al-Diwaniyah General Hospital in collaboration with the Surgical and Laboratory staff, and then transferred to the Parasitology Laboratory at Al-Qadisiyah University in a cold box (Simport, Canada) within 3 hours. The outer surfaces of the cysts were sterilized using 70% ethanol (Sigma-Aldrich, USA). After that, 25 ml of cyst fluid was withdrawn using a syringe and placed in cylinders. The sediment containing protoscoles was washed three times with normal saline (Becton Dickinson (BD), USA).

The viability of protoscoles was tested using a 0.1% solution of eosin stain (Thermo Fisher Scientific, USA). After 5 minutes, dead protoscoleces appeared red-purple under a microscope (Leica Microsystems, Germany), while live ones remained unstained. The viability percentage was calculated after counting at least 450 protoscoles. Live protoscolex were transferred to a dark container containing sterile saline (Becton Dickinson (BD), USA) and stored at 4°C for later use.[10]

Preparation of alcoholic ginger extract[11]

Ginger (Z. officinale) was collected from the local market in Diwaniyah province, Iraq. 500 g of ginger powder was extracted using 70% ethanol. 100 g of powder was titrated into 400 ml of 70% ethanol and mixed for 1 h using a magnetic stirrer (IKA Works, Germany). The solution was left for 24 h at room temperature, then filtered. The solvent was removed using a rotary evaporator (Butchi, R-300, Switzerland), resulting in a non-alcoholic extract of 7.30 g.

Preparation of Niosomes loaded with ginger extract[12]

Ginger extract-loaded niosomes were prepared using a precision digital balance (Metter Toledo, MS2045, Switzerland) to determine the weights of Span 60 (Sigma-Aldrich, S3376, USA), Tween 60 (Sigma-Aldrich, P1629, USA), and cholesterol (Sigma-Aldrich, C8667, USA). 1%-3% ginger extract and 10 ml chloroform (Merck, 102445, Germany) were added. The components were placed on a magnetic stirrer (IKA, C-MAG HS7, Germany) for 45 min to ensure homogeneity, and then in a water bath (Memmert, WNB14, Germany) at 60 °C. Chloroform was removed using a rotary evaporator (Butchi, R-300, Switzerland) to form niosomes as a thin film. Then, the flask was placed in a vacuum oven (Memmert, VO400, Germany) at 60 °C for 4–8 h to completely remove the solvent. 10 ml of phosphate buffer solution (Gibco, 10010023, USA) with pH 7.4 was added, and the flask was placed in an ultrasonic bath (Branson, 2510, USA) at 60 °C to reduce the particle size and form monolayer niosomes. The solution was stored in aluminum-coated glass vials (Schott, DURAN, Germany) at 4 °C to prevent exposure to light and maintain stability.

Determination of in vitro effects of therapeutic compounds[10,13]

The effects of different therapeutic compounds on the protoscole were tested using concentrations (5, 10, 20, 30, 50, 100, 150 mg/ml) of each extract, with incubation periods ranging from 5 to 60 minutes. To prepare these concentrations, 0.1, 0.3, and 0.5 g of the dry extract were dissolved in 10 ml of distilled water (Milli-Q, Merck, USA). In each experiment, 2.5 ml of each concentration was placed in a test tube containing 5000 protoscole (5×10^3), and the appropriate therapeutic compound was added (free ginger extract, niosome loaded with ginger extract, synergistic compound of praziquantel with niosome, and praziquantel alone). The tubes were incubated in an incubator at 37 °C (Thermo Fisher Sentific, Heraeus B6060, Germany).

To ensure the accuracy of the results, ten tubes were designated as a control group by adding 2 ml of distilled water to each tube. The experiments were

repeated for each drug three times, each time in triplicate. After each incubation period, the upper part of the solution was carefully discarded, and 1 ml of 0.1% eosin stain was added to the protoscolices and gently mixed. After 5 min, the upper part was discarded again, and a smear of the protoscolices was placed on a glass slide and examined under a microscope to determine viability.

Statistical Analysis

The data were analyzed using statistical models such as linear and multiple regression and polynomial model to gain insights into the effect of treatment concentrations on the viability of primary heads over specific time periods. ANOVA 1-way test was used to test for differences between concentrations, and ANOVA TUI and Tukey test were used to compare treatments. Analyses were performed using Python and plots were drawn using GraphPad Present.

RESULTS

Evaluating the effect of concentrations of therapeutic compounds on the eradication of protozoan heads during the specified periods: The results showed that the eradication of protozoan heads varies significantly with different concentrations of praziquantel. The concentration of 100 mg/ml achieved 100% complete eradication after 60 minutes, while the lowest concentration of 5 mg/ml achieved 53% extermination in the same period. An increase in eradication rates was also observed after 20 minutes, indicating the importance of time in enhancing the effect of the drug.

The data were statistically analyzed using a linear regression model, which showed that the independent variables (concentration and time) significantly affected the eradication rate. The R-value was = 0.9782, which means that the model explains 97.8% of the variance in the treatment efficacy. The F value = 42.1 also showed high statistical significance at a probability level of $p < 0.05$. ANOVA was also used to verify the significance of the results, and confirmed that the experiment was significant with F = 0.0011 and $p<0.05$, indicating the effect of the drug concentration and time periods on the vitality of protoscolices. Figure (1) supports the results through a graph that shows the relationship between the different concentrations of the drug and the times, with the inclusion of the linear regression equation and the value of the coefficient of determination that confirms the accuracy and efficiency of the model. The concentrations of 50 and 100 mg/ml achieved 100% blackhead regeneration of the primary heads after 60 minutes, while the 5 mg/ml achieved 52% complete regeneration.

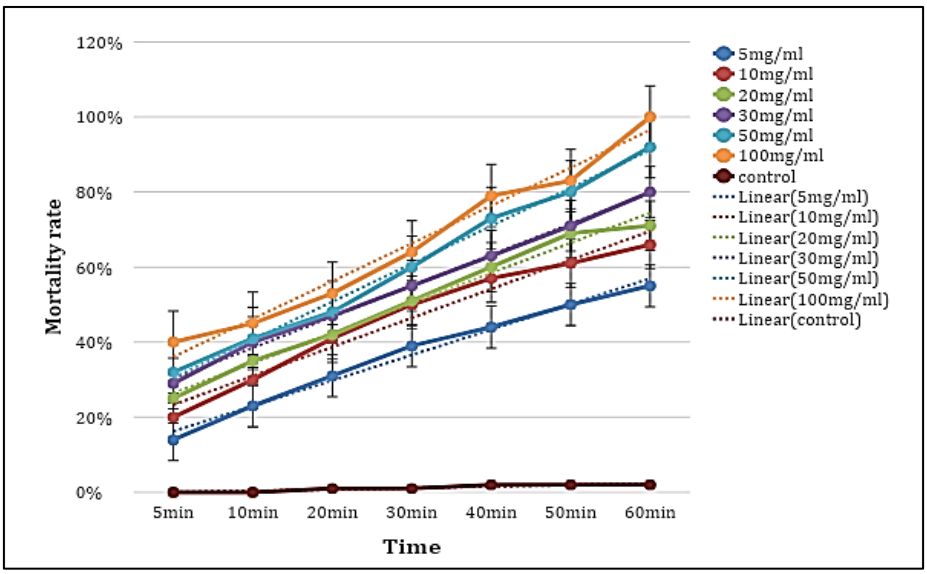

Fig. 1: The Effect of Different Concentrations of Praziquantel on the Vitality of Protoscolices In Vitro at Specific Periods

In addition, there was a new increase in genocide with increasing concentration and time. Statistical analysis using the linear regression model showed that 2.88% of the variance could be explained by the uses (concentration and time), with statistical significance ($F=146.2$, $P<0.05$). The ANOVA test also supported that the concentrations were the main factor in the variance of the results (Figure 2). For Niosom loaded with ginger extract, the concentrations of 50 and 100 mg/ml achieved complete (100%) eradication after 50 min, while the 5 mg/ml concentration achieved 59% eradication at 60 min. There was a gradual increase in

eradication with increasing concentration and time. Statistical analysis using the multinomial model (R=1185.0) showed statistical significance and normal distribution of the data. ANOVA analysis also showed that concentrations and periods had a significant effect on the results (F=11.82, P<0.05) (Figure 3).

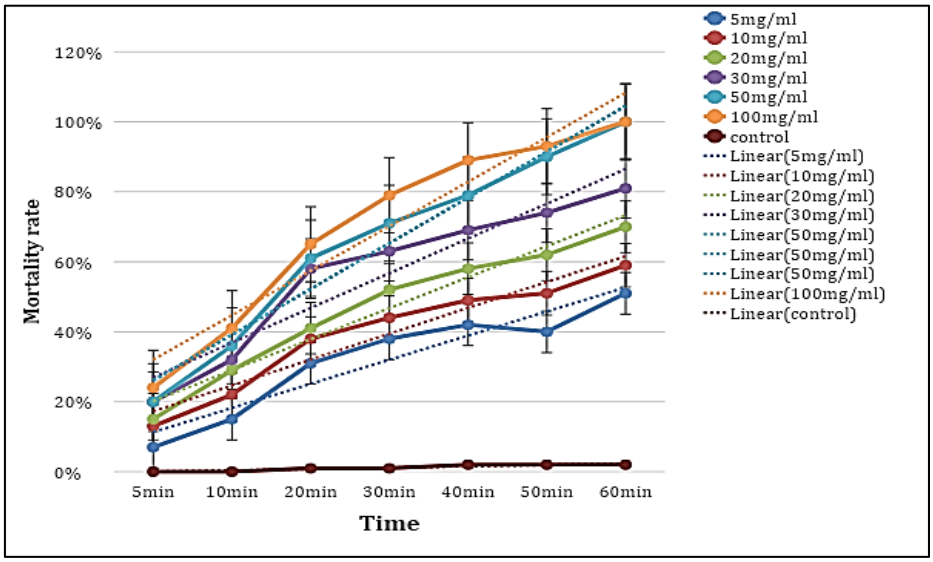

Fig. 2: The Effect of Different Concentrations of Ginger Extract on the Vitality of Protoscolices In Vitro at Specific Periods.

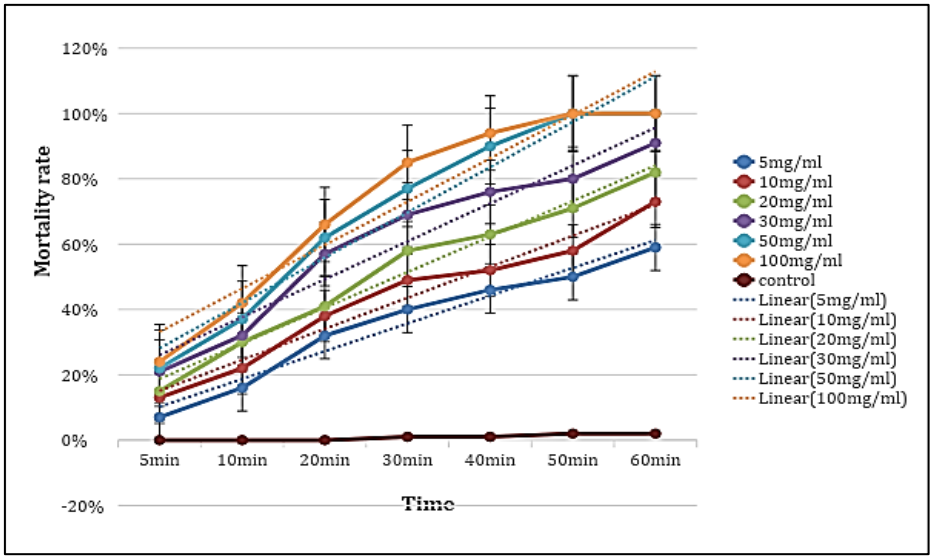

Fig. 3: The Effect of Different Concentrations of Ginger Extract-Loaded Niosomes on the Vitality of Protoscolices In Vitro at Specific Periods.

The 50 and 100 mg concentrations of the synergistic compound of praziquantel and niosom loaded with ginger extract resulted in complete eradication (100%) after 40 min, while the 5 mg concentration achieved 63% eradication at 60 min. The eradication rates ranged from 63% to 100% with a gradual increase depending on the concentration and time. Statistical analysis showed that the model explained 93.5% of the variance in the data (R=0.935). The results also showed a positive relationship between concentrations and time, with a statistically significant effect of concentration, while time did not show a significant effect at all periods (figure 4).

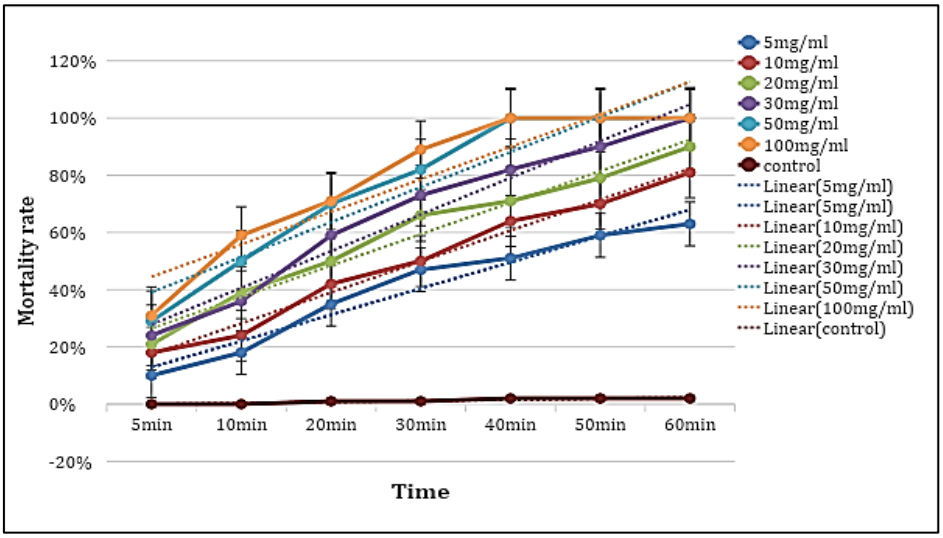

Fig. 4: The Effect of Different Concentrations of the Synergistic Compound on the Vitality of Protoscolices In Vitro at Specific Periods.

Relationship between the therapeutic compounds concentrations and the rates of protoscoles extermination:

The results of the statistical analysis showed that the synergistic compound of niosom loaded with ginger extract was superior in killing primary heads by 79% within 60 minutes, outperforming the rest of the compounds. The rates of extermination of praziquantel ranged between 66% and 79%, while the rate of extermination of ginger extract was between 32% and 40% at a concentration of 5 mg/ml. The descriptive analysis showed that the overall mean of the results was 92.44 and the standard deviation was 11.89, indicating significant differences between the different treatments ($p<0.05$).The ANOVA test showed significant differences between the compounds with $F=11$ and $P<0.00018$. Paired t-tests revealed significant differences between the synergistic compound and praziquantel ($t=-4.710$, $p<0.0008$) and the synergistic compound and ginger extract ($t=-5.239$, $p<0.0004$). No significant differences were found between the ginger-loaded niosomes and the synergistic compound ($t=-1.54$, $p<0.154$) (Figure 5).

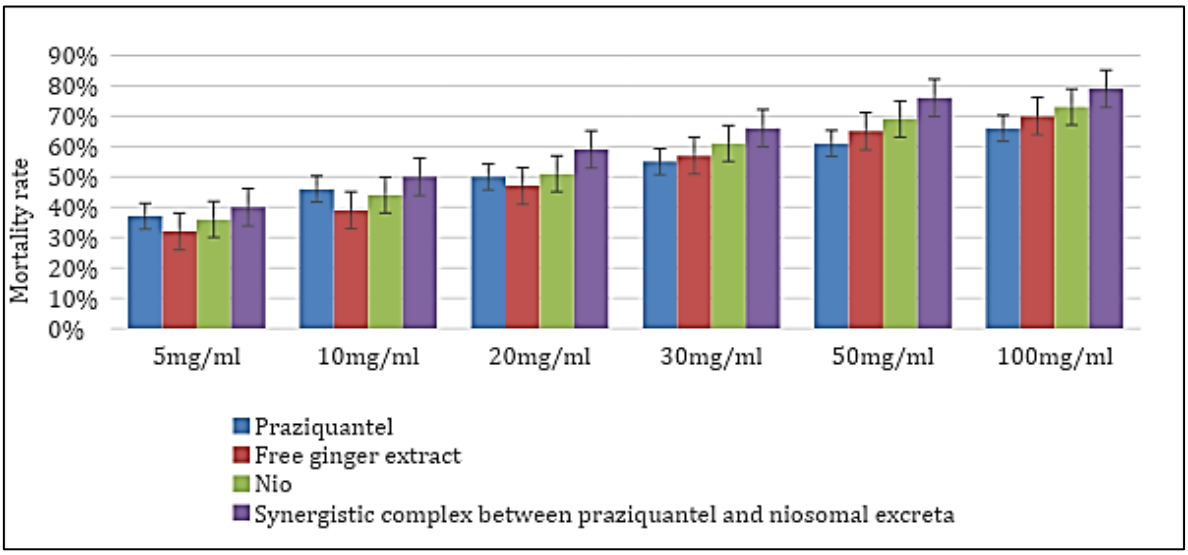

Fig. 5: Illustrates the effect of different concentration levels of the therapeutic compounds under investigation on the vitality of protoscolices after 60 minutes of exposure

DISCUSSION

The present study focus on evaluating the effect of different concentrations of a therapeutic compound on the viability of protozoan parasites in the laboratory using an experimental design that studies the effect of each treatment separately. The results showed variation in the efficacy of treatments across different concentrations and periods, which emphasizes the importance of studying each treatment separately before comparing treatments. A gradual increase in the percentage of protoscolices parasite exterminate was extermination with increasing drug concentration and exposure period. Praziquantel at a concentration of 100 mg showed a complete extermination 100% at minute 60 of the experiment. Linear regression analysis also showed a strong relationship between drug concentrations and eradication rate, with an R-squared value of 0.98771 demonstrating the model's ability to explain the variation in extermination rates. The results of the analysis of variance (ANOVA) also confirmed the presence of statistically significant differences between drug concentrations, which supports the hypothesis of a significant effect of drug concentration on extermination. These results are consistent with previous studies[14,15] that showed that praziquantel inhibited the growth of protozoan parasites and prevented the formation of hydatid cysts. They are also consistent with the study that confirmed the efficacy of praziquantel in treating hydatid cysts[16]. Despite the positive results, in vitro, additional studies are needed to verify the drug's effect in vivo. Praziquantel is the preferred treatment for intestinal parasites in dogs, and has been the WHO-approved treatment for schistosomiasis for 40 years.[17]

However, current results are still insufficient to approve praziquantel for direct use in humans, and increasing concentrations in in vivo studies should be limited to avoid side effects. The present results documented the effectiveness of the alcoholic ginger extract in Extermination protoscolex, as concentrations of 50 mg/ml and 100 mg/ml achieved complete eradication of 100% after 60 minutes. The concentration of 50 mg/ml was the optimal one, as it achieved complete eradication earlier than the rest of the concentrations. Linear regression analysis showed a strong relationship between the extract concentration and the eradication rate, with R = 0.98642 explaining 98.6% of the variance in the results. The results of the ANOVA test also showed a statistically significant difference between the different concentrations of the extract. These results are consistent with previous studies, which confirmed that alcoholic ginger concentrations of 100, 150, and 200 mg/ml achieved complete extermination protoscolices at rates of 92.3%, 93%, and 100%, respectively, over time periods ranging from 15 to 60 minutes[18].

The present study explores the effectiveness of niosomes loaded with ginger extract in extermination protoscolex, as the results showed high complete exterminating ability at two concentrations of 50 and 100 mg/ml after 60 minutes of the experiment. Polynomial regression analysis showed a strong relationship between concentrations and extinction rates, with R = 0.981, indicating that 98% of the variance could be explained by the model. Omnibus = 0.410 and prob Omnibus = 0.816 showed no significant deviations from the normal distribution of the residuals, while Durbin-Watson = 1.981 indicated no serial correlation between the residuals, strengthening the validity of the model.

The results of the ANOVA test showed a value of F = 12.98 at $p<0.05$, indicating high statistical significance for the observed effects of different doses on protozoan parasites. These results strongly support the experiment and confirm the validity and use of the model to correctly interpret the data. These results are consistent with previous studies[18], which shows beneficial effects of nano-curcumin complexes on protozoan parasites in vitro.

This study focused on the synergistic effect of a complex of praziquantel with niosomes loaded with ginger extract on protozoan parasites in vitro. Results showed that the coupling tool had an accuracy ranging from 63% to 100% with a gradual non-linear increase over time. Complete antibody responses varied from 50 to 100 mg at 40 minutes, whereas a lower dose (50 mg) achieved a 63% response at 60 minutes. Polynomial regression modeling indicated that the model was able to explain 89% of the data variance, supporting a positive relationship between different levels of cooperation proteins. These results are consistent with previous studies which showing that a combination of albendazole and otovaccine produced a better protoplasty inhibition than albendazole alone and supports the finding that the combination of albendazole sulfoxide is beneficial in inhibiting protocol at low concentrations , and this is a great way to reduce the side effects of albendazole[19,20] .

Taking both drugs together is an effective way to improve the treatment efficacy of both drugs. This is because the interaction of the two drugs enhances the effect of the combination and increases the effectiveness of both drugs. and reduce the risk of side effects that may occur There are several studies supporting this hypothesis, such as studies by Sarmadian *et al*, [21,] ; Roell *et al.* [22] that emphasizes the importance of synchronization in complex cases such as hydatid tumors. This is considered safe to induce with chemotherapy because of side effects.

Effects of various concentrations Antimicrobial viability was determined for periods ranging from 5 to 60 minutes in standard experiments. The results show that the interactive solution achieves higher performance. This is because 100% more particles are removed than other treatment solutions. In contrast, praziquantel is less effective. As rejection rates ranged from 66% to 79%, all therapeutic compounds generally showed elimination efficiency. But there are clear differences in effectiveness, this is because effects will vary depending on the size of each compound and its specific components. It was also found that increased concentration was accompanied by increased degradation rate. But the compound's efficacy remained the highest for all compounds tested, with praziquantel being less effective.

Analysis of variance (ANOVA) was used to test the existence of significant differences between the effects of each concentration on protocol at 60 min. The results showed significance, $F = 54.23$. at $p < 0.0098$, which indicates that the drug effects are statistically significantly different. This indicates that the type and number of factors affect the accuracy value. Differences between groups were analyzed by T-test, and the results showed that there were statistically significant differences among the four treatment compounds at a significance level of less than 5%. The synergistic combination with niosomes at Adding ginger oil has the highest rate of decomposition. Followed by alcohol extract from ginger. and praziquantel, which has the lowest rate of degradation. Significant differences in the intensity of treatment combined with other treatments It clearly demonstrated superiority in terms of efficacy in extinguishing protozoa. However, it appears that the companion extract added with ginger oil is an effective and reasonable option for treating patients with stable symptoms, while companion extracts are recommended for advanced stage patients, when a tumor spreads throughout various organs[22].

The standard deviation results indicate that the niosome loaded with ginger extract shows greater stability and balance compared to praziquantel and ginger alcoholic extract, so it is recommended for treating moderate cases due to its balanced effectiveness and limited side effects. These results support the conclusions that choosing the most appropriate therapeutic compound depends on the type of infection and the concentration of the therapeutic compound to achieve the best results in eliminating protoscolices.

CONCLUSIONS

All compounds under study were effective in extermination of protoscolices gradually with increasing concentration and time, with the synergistic compound being the most effective, followed by niosome loaded with ginger extract, while praziquantel was less effective. The data show that the efficacy of the synergistic compound was less stable, making it better to limit its use as a treatment to acute cases that require rapid intervention. On the other hand, niosome loaded with ginger extract was more stable, and therefore, niosome is the most suitable option for treating cases that require continuous monitoring or in non-acute cases of hydatid cysts.

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REFERENCES

1. Al-Khalidi KA, Al-Abodi HR, Jabbar HK, Hmood BA. Echinococcus granulosus. InOverview on Echinococcosis 2020 Mar 4. IntechOpen.
2. Al-Abodi HR, Al-Shadeedi SM, Al-Alo KZ, Ghasemian A. Zataria Multiflora bois as an auspicious therapeutic approach against Echinococcus granulosus: current status and future perspectives. Comparative Immunology, Microbiology and Infectious Diseases. 2019 Oct 1;66:101335.
3. Alshoabi SA, Alkalady AH, Almas KM, Magram AO, Algaberi AK, Alareqi AA, Hamid AM, Alhazmi FH, Qurashi AA, Abdulaal OM, Aloufi KM. Hydatid disease: a radiological pictorial review of a great neoplasms mimicker. Diagnostics. 2023 Mar 16;13(6):1127.
4. Aminpour S, Rafiei A, Jelowdar A, Kouchak M. Evaluation of the protoscolicidal effects of albendazole and albendazole loaded solid lipid nanoparticles. Iranian journal of parasitology. 2019 Jan;14(1):127.
5. Hmidi M, Touiheme N, Rbai M, Messary A. Isolated hydatid cyst of the neck: an unusual site. European annals of otorhinolaryngology, head and neck diseases. 2012 Apr 1;129(2):108-10.
6. Rajabi MT, Berijani S, Amoli FA, Mohammadi SS. Hydatid cyst of inferior rectus. Ophthalmic Plastic & Reconstructive Surgery. 2021 May 1;37(3S):S168.

7. Kumar V, Surve A, Biswal D, Verma N, Kashyap S, Venkatesh P, Mirdha BR. Intra-ocular hydatid cyst in a child: A rare presentation. European Journal of Ophthalmology. 2023 May;33(3): NP70-4.
8. Jeziorski MC, Greenberg RM. Voltage-gated calcium channel subunits from platyhelminths: potential role in praziquantel action. International journal for parasitology. 2006 May 31;36(6):625-32.
9. Garedaghi Y, Sperança MA, Ghimire TR, Khan W. Drug Treatment of Hydatid Cyst With Albendazole and Praziquantel in Humans. Int J Med Parasitol Epidemiol Sci Volume. 2021;2(3):63.
10. Mares MM, Al-Quraishy S, Murshed M. Effectiveness Evaluation of Viti's vinifera Leaf Extract on the Viability of Echinococcus Eggs and Protoscolices In Vitro. Veterinary Sciences. 2023 Jun 18;10(6):400.
11. Almalki E, Al-Shaebi EM, Al-Quarishy S, El-Matbouli M, Abdel-Baki AA. In vitro effectiveness of Curcuma longa and Zingiber officinale extracts on Echinococcus protoscoleces. Saudi journal of biological sciences. 2017 Jan 1;24(1):90-4.
12. Samaei SS, khanmohammadi Khorrami M, Garmarudi AB. Investigation the application of niosome as a nanocarrier for sage (Salvia officinalis L.) extract by spectroscopy and chemometrics. Revista del Cuerpo Médico Hospital Nacional Almanzor Aguinaga Asenjo. 2021 Aug 24;14(2):155-62.
13. Huang H, Fang HB, Tan MT. Experimental design for multi-drug combination studies using signaling networks. Biometrics. 2018 Jun;74(2):538-47.
14. Hemphill A, Rufener R, Ritler D, Dick L, Lundström-Stadelmann B. Drug Discovery and Development for the Treatment of Echinococcosis, Caused by the Tapeworms Echinococcus granulosus and Echinococcus multilocularis. Neglected Tropical Diseases: Drug Discovery and Development. 2019 Sep 30:253-87.
15. Richter J, Lindner AK, Geisel D, Torsello GF, Martinez GE, Isner C, Schürmann D, Pfäfflin F, Orhun A, Manciulli T, Brunetti E. Treatment of a giant hepatic echinococcal cyst with percutaneous drainage and in vivo assessment of the protoscolicidal effect of praziquantel. Clinical journal of gastroenterology. 2021 Jun;14:888-92.
16. Garedaghi Y, Sperança MA, Ghimire TR, Khan W. Drug Treatment of Hydatid Cyst With Albendazole and Praziquantel in Humans. Int J Med Parasitol Epidemiol Sci Volume. 2021;2(3):63.
17. Tadele T, Astatkie A, Tadesse BT, Makonnen E, Aklillu E, Abay SM. Efficacy and safety of praziquantel treatment against Schistosoma mansoni infection among pre-school age children in southern Ethiopia. Tropical Medicine and Health. 2023 Dec 20;51(1):72.
18. Teimouri A, Jafarpour Azami S, Hashemi Hafshejani S, Ghanimatdan M, Bahreini MS, Alimi R, Sadjjadi SM. Protoscolicidal effects of curcumin nanoemulsion against protoscoleces of Echinococcus granulosus. BMC Complementary Medicine and Therapies. 2023 Apr 18;23(1):124.
19. Sadr S, Lotfalizadeh N, Abbasi AM, Soleymani N, Hajjafari A, Roohbaksh Amooli Moghadam E, Borji H. Challenges and prospective of enhancing hydatid cyst chemotherapy by nanotechnology and the future of nanobiosensors for diagnosis. Tropical medicine and infectious disease. 2023 Nov 6;8(11):494.
20. Enkai S, Kouguchi H, Inaoka DK, Irie T, Yagi K, Kita K. In vivo efficacy of combination therapy with albendazole and atovaquone against primary hydatid cysts in mice. European Journal of Clinical Microbiology & Infectious Diseases. 2021 Sep;40:1815-20.
21. Sarmadian R, Shafiee H, Bayatiani M, Rokni M, Ghasemikhah R. Synergistic effect of focused ultrasound and albendazole sulfoxide on hydatid cyst protoscolices in vitro. Available at SSRN 4161380. 2023.
22. Roell KR, Reif DM, Motsinger-Reif AA. An Introduction to Terminology and Methodology of Chemical Synergy—Perspectives from Across Disciplines. Front Pharmacol. 2017; 8 (158) [Internet]. 2017.