Iraqi Journal of Industrial Research (IJOIR)

Journal homepage: http://ijoir.gov.iq

Preparation and Evaluation of Mebendazole 5% Antiparasitic Suspension for Veterinary Use

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Article information

Article history:
Received: June, 28, 2022
Accepted: August, 08, 2022
Available online: October, 20, 2022

Keywords:
Mebendazol,
Gastro-intestinal infection,
Antiparasitic

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DOI:
https://doi.org/10.53523/ijoirVol9I2ID242

Abstract

The purpose of this study is to prepare a new formulation of Mebendazole suspension for veterinary therapeutic and antiparasitic use at a concentration of 5% of the poorly water soluble drug mebendazole using suspending agents, dispersing agents such as tween 80, polypropylene glycol, preservatives, and other salts to titrate the PH of the resulting mixtures. Information about all the materials used in the preparation of the formula was collected from pharmacopeia, while materials were provided by Samarra Company. and prepared about three formulae, from which the final one prepared. A study was conducted on the stability of the new formula in different temperature conditions (40, 50, and 60) °C by comparing any change in physicochemical properties concerning form, viscosity, and pH in different storage rooms and other temperatures for 18 months. showed that The results of the new drug proved its stability, both quantitative and qualitative results for suspension 5% formula as well as its physicochemical properties and viscosity tested and also conducted clinically therapy in the central veterinary hospital the findings demonstrate that Mebendazol is a promising new formulation of it for treatment of hydatid diseases without showing significantly liver toxicity.

1. Introduction

Mebendazole is a synthetic benzimidazole and belongs to the group of benzimidazoles. Figure (1) [1]. Parasitic helminthes affect people and animals around the world. They have a significant impact on growth, production (wool, eggs, milk, etc.), and overall resistance to other diseases. Different parasites infect our domestic animals and cause great losses. Mebendazole has a wide spectrum of anthelmintic activity and is a highly effective broad spectrum antihelmintic indicated for the treatment of nematode infestations, including roundworm, whipworm, threadworm, and hookworm. It is also highly effective in the treatment of hookworm and trichuris infections. When administered orally, only around 10% of the mebendazole is absorbed, with peak plasma concentrations after 1 or 2 hours. It has a short plasma half-life of 2.5 to 5.5 hours [2]. Three polymorphic forms of mebendazole, identified A, B and C can beformed through controlled crystallisation procedures. Polymorph C is apparently pharmaceutical favored [3]. The dose of mebendazole (100 mg mebendazole twice a day for three consecutive days) is shown to be very effective in the treatment of hookworm and trichuris infections [4]. Mebendazole is poorly soluble in water, which benefits the action against gastro-

intestinal helminthes and Since mebendazole is poorly absorbed from the gastro-intestinal tract at the usual therapeutic doses, side effects have generally been restricted to gastrointestinal disturbances such as abdominal pain and diarrhoea [5]. Mebendazole is an anthelmintic with a broad spectrum of action. Mebendazole works locally in the gut lumen by interfering with cellular tubulin formation in worm intestines. Mebendazole binds to tubulin specifically and causes ultrastructural degeneration in the intestine. As a result, the worm's glucose uptake and digestive functions are disrupted to the point where an autolytic process occurs [6].

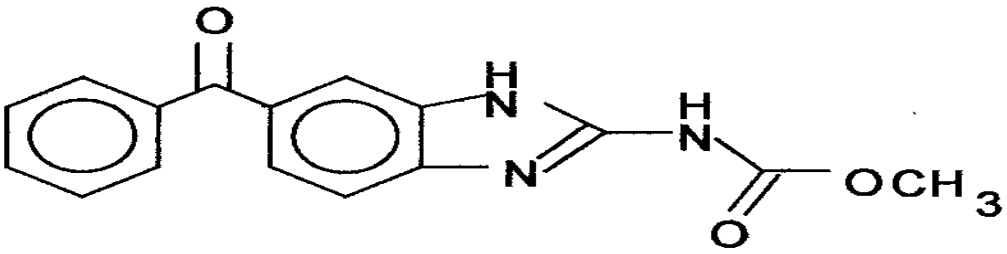

Figure (1). Chemical name of mebendazole [5-Benzoyl-lH-benzimidazol-2-yl)-carbamic acid methyl ester.

2. Material and Methods

2.1. Chemical Compounds

Menbendazole, suspending agent, dispersing agent, preservative, ethanol, salt, wetting agent was provided as sample from SDI company and Distilled water and specification of ingredient in Table (1).

Table (1)**.** Specification of component of mebendazole suspension.

N	Substance	Specification	Description	Solubility
1	Mebendazol	[7]	agrey-white to pale yellow powder	not sol.in water and organic solvent
3	Suspending agent	[8]	A cream coloured	
4	Wetting agent	[8]	A clear, colourless	miscible with water and with ethanol
5	Dispersing	[7]	Aclear oily yellowish ,or brownish - yellow liquid	miscible in all proportion with water
6	Preservative	[7]	Colourlees crystals, white crystalline	soluble in 500 part of water and in 3.5 part of ethanol
7	Preservative	[7]	whit,crystallinodourless with afainty	
8	Ethyl alcohol	[7]	Acdourless , clear , mobile	miscible with water and with ether
9	Wetting agent	[7]	Aclear,colourless viscous liquid	miscible with water
10	Acid	[7, 8]	colourless , crystal , or awhitle	soluble with water
11	Base	[7, 8]		

2.2. Apparatus

sieve at mesh 250µ, Magnetic starrier hotplate, mixer for liquid, balance, pH meter, heater, filter paper and different glasses (volumetric beaker, cylinder, volumetric flask and conical flask).

2.3. Preparation of Mebendazol Suspension

As the maximum stability of mebendazol has been observed of pH = 5.5 therefore it was necessary to use basic in order to provide the mentioned PH. All the powders were passed through 2.5 mesh. Required quantities of

Mebendazole. suspension which were in estimated in this study contained 5mg /100ml (5%w/w) of mebendazol and amount of suspending 1.5g, also 0.5g other as suspending agents Table (1) were used as preservative agents. the wetting agent was used of concentration of 3%w/v for the preparation of suspension the suspending agent was initially dispersed in prepared dispersing solution contain from dispersed with water. In the next step, mebendazol which was wetted by wetting agent was added to the vehicle and dispersed by tumbling for 10 minutes. the suspension of prepared were transferred to 100ml amber glass bottles with well-sealed covered and stored of room temperature under static conditions.

1. PH determination: The PH of all developed formulations was measured using digital PH meter.
2. Determination of viscosity: The Viscosity of suspension samples was determined using the Brookfield viscometer at 100 rmp. All determination was carried out in at least triplicates and result obtained were expressed as the mean values.
3. Effect of temperature: Further the effect of the temperature (30° to 60°) was investigated on the viscosity of the suspension of all formulation.

2.4. Procedure

physical stability test: sedimentation volume (f) was measured in 100ml graduated glass cylinders, the sedimentation volume was recorded of 1, 2, and 7 months' storage periods for three sample of each formulation sedimentation volume was expressed as the ratio between the height of sediment of the specified time of evaluation and the height of the suspension of the time.

Table (2). The formulae for preparation of suspension.

Ingredients Meb. Formula	**Formulation Code** F M_1	FM_2	FM_3	FM_4
Mebendazole	5gm	5gm	5gm	5gm
Dispesing agent	0.01gm	0.02gm	0.04gm	0.05gm
Suspending agent	1gm	0.015gm	0.018	0.2gm
Suspending agent	1.5gm	1.25gm	1.3gm	1.5gm
Salt	0.0135	0.0135	0.0135	0.0135
Basic	–	–	–	–
Salt	0.05gm	0.05gm	0.05gm	0.05gm
Preservative	0.07gm	0.07gm	0.07gm	0.07gm
Preservative	0.03gm	0.03gm	0.03gm	0.03gm
Wetting agent	3ml	3.5ml	3.5ml	5ml
Wetting agent	2ml	2ml	2ml	2ml
Ethyl alcohol	1ml	1ml	1ml	1ml
acid	0.05gm	0.05gm	0.05gm	0.05gm

3. Results and Discussion

The suspension different formulations were prepared using suspending agent. Their combination to give good formula for avoiding precipitation of mebendazole on dilution in the gut lumen to choose FM1 the suspension was prepared from because the mebendazol is practically insoluble in water and has poor wettability. Many poorly water soluble as shown Table (1). in this study conduct the test pure Mebendazole and mixture of Mebendazole suspension shows similar with slightly deviations in the drug of formula indicating the chemical stability of the drug. Shows that percentage of activity between 96.6% and 100% according British pharmacopeia for six months under different temperature degree at (25, 40, 50, and 60°C), respectively with slightly deviation with compared in zero time and other time of mebendazol Table (2).

Table (3). chemical analysis of 5% mebendazole suspension after storage in different temperature for 6months with biological assay.

Date and Time of analysis	Activity of solution after storage at 25ºC "Room Temperature"	Activity of solution after storage at 40ºC	Activity of solution after storage at 50ºC	Activity of solution after storage at 60ºC
zero time	100%	100.2%	100.1%	100%
After one month	100%	100. %	100%	99.1%
After two month	99%	98.84%	98. 75 %	98 .65%
After three month	98.55%	98.50%	98.45%	98.40%
After four month	98.40%	98.35%	98.25%	98.15%
After five month	97.9%	97.84%	99.84%	97.75%
After six month	97%	96.99%	96.98%	96.6%

Table (4). The evaluation of mebendazol suspension pH.

Time of pH	**degree of suspension after storage at 25ºC "Room Temperature"**	**degree of suspension after storage at 40ºC**	**degree of suspension after storage at 50ºC**	**Degree of suspension after storage at 50ºC**
zero time	6.5	6.5	5	5
After one month	6.5	6	5.5	5.5
After two month	6.9	6.5	6	5.9
After three month	6.5	6.5	6.5	6.5
After four month	6.5	6.5	6.5	6
After five month	6	5.99	5.97	5.95
After six month	5.95	5.92	5.90	5.50

The pH control as an important role in stability control of suspension in order to avoid coagulation and in stability .At the lower pH [acidic condition) and higher pH (alkaline condition) shown as Table (3), The results showed that the reduction rate of cyst weight induced by (mebendazole suspension) MBZ at two doses was

95.23% and 92.67%, which was significantly higher than that of MBZ 1% suspending (positive control) at corresponding concentrations (87.41% and 69.47%), indicating that the treatment over the past 30 years showed that the evaluation of therapeutic effectiveness was overestimated; thus, 40% of all parasitic larval . The original oil micronized mebendazole suspension tested by us in. The administration of MBZ-OS resulted in a treatment efficacy with the cyst weight reductions higher than 80%, significantly better than the corresponding mebendazol 1% suspending groups. Observed at Table (5) the viscosity and spread ability decrease with increase storage temperature degree due to must be storage the product between 25°C and 30°C. The better treatment efficacy of mebendazol [9] was related to the higher drug concentration in plasma, parasites and tissues the treatment of hydatid diseases, the benzimidazoles were considered safe with occasional side effects [10, 11].

Table (5). Caption should be in the same font and size of the text.

Formulation Code	Parameter of cream	25Cº 65% RH	30Cº 65% RH	40Cº 65% RH
	The viscosities(CPS)	**33.5**	**32**	**31.9**
	Spreadability(g/sce)	**43.9**	**43.3**	**42**

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