

A Practical Approach for Solubility Enhancement of Albendazole

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ABSTRACT

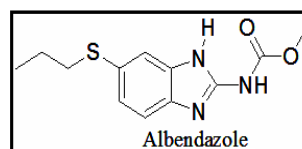
Albendazole is an anti-helminthic or anti-worm medication. Due to its water insolubility, it shows poor absorption in GIT as well as low bioavailability and produces poor therapeutic effect. In this study, various hydrotropic agents are used to enhance the solubility of Albendazole. Addition of 100 mg of Albendazole to the 1M Solution of hydrotropic agent like Sodium benzoate, Sodium acetate, Sodium citrate, Sodium salicylate & urea separately and absorbance of each solution at wavelength 306nm was determined. Results shows an increment in solubility of Albendazole and also percentage drug release increased upto 19.8%, 25.9%, 26.5% 73.2%, 75.2%, 76.5% and 80.7% using 1M solution of Sodium benzoate 100 mL, Sodium benzoate 50 mL, Sodium benzoate+Urea (25 mL+25 mL), Sodium citrate 50 mL, Sodium acetate 50 mL, Urea 50 mL and Sodium salicylate 50 mL respectively. As sodium salicylate has an aromatic ring with an electron donating Hydroxyl group that lacks in other hydrotropic agent used, may be responsible for increase in solubility as well as drug release of Albendazole up to 80.7%.

Keywords: Albendazole, Anthelmintic, Hydrotropy, Solubility enhancement, Hydrotropic agents.

INTRODUCTION

Albendazole, methyl[5-(propylthio)-1-*H*-benzimidazol-2-yl] carbamate is a Benzimidazole derived compound having a wide range of effectiveness against human being and animal helminth parasites. Albendazole is effective in the treatment of echinococcosis, hydrated cysts and neurocysticercosis. Albendazole is a poorly water soluble drug. Consequently, it is poorly absorbed from the gastrointestinal tract (< 5%) and it has low oral bioavailability.¹ Solubility, particularly in the aqueous system, is an important physicochemical property of a medicinal ingredient. For therapeutic efficacy, a medication must have some aqueous

solubility. A drug must first be in solution before it may enter the systemic circulation and have a therapeutic effect. Absorption of somewhat insoluble substances is frequently partial or irregular. If the drug substance's solubility is less than ideal, it must be considered to improve its solubility.²



Factor affecting solubility

Size of particle, Pressure, Type of solvent and solute used, polarity of solvents.

Helminthiasis

Helminthiasis is one of the most common animal illnesses, causing significant output losses. Due to poor helminthiasis management procedures, the disease is very common, especially in third-world nations.³ Helminthiasis is one of the most frequent infections in humans, affecting a huge percentage of the global population. They are a significant hazard to public health in impoverished nations, contributing to malnutrition, anaemia, eosinophilia, and pneumonia.⁴ Helminth infections are the most common parasite illnesses in animals. Cestodes (tapeworms), nematodes (roundworms), and trematodes are three forms of cestodes (liver flukes). Anthelmintic drugs, which are necessary for sustaining high weight increases and reproductive performance in livestock, are used to control helminth infections.⁵

Disease condition

Helminthic infections are especially common in people who live in poverty and do not maintain a sanitary environment. Helminths are primarily found in tropical areas, where they pose a major health risk by contributing to malnutrition, anaemia, eosinophilia, and pneumonia.⁶ Most of worm infections occur in tropical places; but, they can also arise in travellers who have visited those areas, and some of them can develop in temperate climates. In this disease the hygienic condition should be maintained and its very impotent.⁴

Techniques of solubility enhancement

Some techniques used in solubility enhancement are Salt Formation, Co-crystallization, Co-solvency, Hydrotropic, Solubilizing agent, Nanotechnology, Particle size reduction, Micronization, Nano suspension, Modification of the crystal habit, Complexation, Solubilization by surfactants, Micro emulsions, Self micro emulsifying drug delivery system and Drug dispersion in carriers.

Hydrotropy

Hydrotropy is a solubilization process in which a large amount of a second solute causes the aqueous solubility of a third solute to increase. Many poorly water-soluble medications have been reported to benefit from concentrated aqueous hydrotropic solutions of sodium benzoate, sodium salicylate, urea, nicotinamide, sodium

citrate, and sodium acetate. A typical example is aqueous injection of caffeine with sodium benzoate (a hydrotropic agent).⁵

MATERIALS AND METHOD

Albendazole obtained from Modern Laboratories Ltd., Indore. Sodium benzoate, Sodium acetate, Sodium citrate and Urea were taken from the Sri Aurobindo Institute of pharmacy, Indore and were of analytical grade.

Calibration curve: (UV method for analysis)

100 mg of Albendazole was dissolved in 75 mL of formic acid in a 100 mL volumetric flask and shake for 30 minutes. After 30 min, make up the volume to 100 mL of formic acid (1 mg/mL). Take 1 mL of solution & dilute it to 10 mL of the formic acid to prepare 100 µg/mL stock solution. Various concentrations of solution (2, 4, 6, 8, 10, 12, 14, 16, 18, 20, & 25 µg/mL) were prepared and labelled. Then measure the absorbance of these all above solutions in ultraviolet spectrophotometer at 306 nm wavelength. Plot a graph between concentration & absorbance (Table no 1).

Comparative solubility analysis with hydrotropic agent

Prepare the 1M Solution of the following hydrotropic agent like Sodium benzoate, Sodium acetate, Sodium citrate, Sodium salicylate & urea. Then add 100 mg of Albendazole in each hydrotropic agent and shake all the solution (Albendazole + hydrotropic agent) for 45 min & filter the solution by Whatman filter paper. Then check the absorbance of each solution at wavelength 306 nm. Then identify the percent drug release. Then plot the graph between % drug release & hydrotropic agent.

RESULT AND DISCUSSION

The objective of this study is to enhance the solubility of the Albendazole which requires to improve the dosage form characteristics. Solubility can be enhanced by variety of technique that leads to an increment in solubility up to its maximum extent. Most of the drugs possess a low solubility profile that causes their less availability in biological environment. This

drawback provides researcher an idea to improve solubility and bioavailability of water insoluble drugs. Hydrotropy is Solubilization method in which the addition of a large amount of second solute is result is in increase in the aqueous solubility of another solute. The hydrotropic agent (sod. benzoate, sod. salicylate, sod. acetate etc.) are solubility enhancer. A hydrotropic agent is compound that solubilize hydrophobic compound in aqueous solution. Typically, hydrotrops consist of a hydrophilic part and a hydrophobic part but the hydrophobic part is too small to cause self spontaneous & self aggregation. The hydrotropic agent lipophilic in nature therefore its use to enhance the solubility of poorly soluble drugs. The hydrotropic solubilization of the Albendazole at minimum hydrotrops concentration leads to weak ionic interaction involving a complexation while that at higher hydrotropic concentration may be due to molecular aggregation and inclusion of one in the aggregate in higher concentration.

The solubility profile of Albenazole is increasing order to Sodium benzoate>Sodium citrate>Sodium acetate>urea>Sodium salicylate. The Sodium salicylate has hydroxyl group which may leads to the hydrogen bonding and formation of aggregation. The Albendazole is a water insoluble drug so the hydrotropy is a method which increases the solubility. In this project following hydrotropic agent sodium benzoate, sodium acetate, sodium salicylate, sodium citrate & urea are used. The hydrotropic agent & drug ratio is (50 mL: 100 mg) respectively and the concentration of the hydrotropic agent is 1M. The sodium benzoate is taken in two different ratios, first 50 mL dissolve 100 mg Albendazole & another 100 mL dissolve 100 mg Albendazole for determination of the solubility. Another agent is used in 50 mL: 100 mg. A mixture of hydrotropic agent area also used called mixed hydrotropic. The ratio of two hydrotropic agents is (Sodium benzoate 25 mL: Urea 25 mL: 100 mg Albendazole). The Albendazole solubility increased in following hydrotropic agent is sodium benzoate (50 mL) 25.9%, Sodium benzoate (100 mL) 19.8%, Sodium 25 mL + Urea 25 mL is 26.5%, Urea

(50 mL) 76.5%, Sodium salicylate (50 mL) 80.7%, Sodium acetate (50 mL) 75.2%, & Sodium citrate (50 mL) 73.2%.

Table 1: Absorbance of Albendazole

S.no	Concentration	Absorbance
1	Blank	0.0
2	2µg/mL	0.138
3	4µg/mL	0.201
4	6µg/mL	0.277
5	8µg/mL	0.305
6	10µg/mL	0.478
7	12µg/mL	0.501
8	14µg/mL	0.508
9	16µg/mL	0.641
10	18µg/mL	0.700
11	20µg/mL	0.792
12	25µg/mL	0.927

Calibration curve of Albendazole

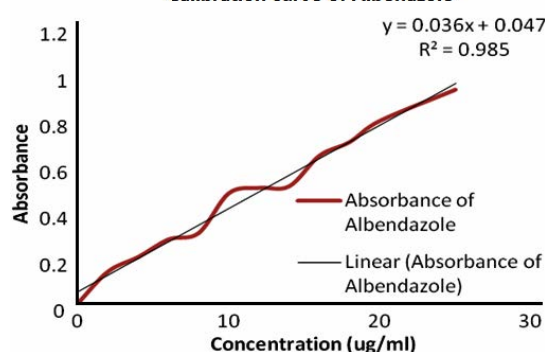


Fig. 1. Calibration curve of Albendazole

Table 2: Solubility study with different hydrotropic agent

S.no	Hydrotropic agent	Concentration	Absorbance
1	Sodium benzoate(50 mL)	1M.	0.42
2	Sodium benzoate(100 mL)	1M.	0.19
3	Sod.Benzoate+urea(25+25 mL)	1M.	0.430
4	Urea(50 mL)	1M.	1.15
5	Sodium salicylate(50 mL)	1M.	1.21
6	Sodium acetate(50 mL)	1M.	1.13
7	Sodium citrate(50 mL)	1M.	1.10

Table 3: Solubility study with increase in concentration of different hydrotropic agent

S.no	Hydrotropic agent	% drug release
1	Sodium benzoate(50 mL)	25.9%
2	Sodium benzoate(100 mL)	19.8%
3	Sod.benzoate+uera(25+25 mL)	26.5%
4	Urea(50 mL)	76.5%
5	Sodium salicylate(50 mL)	80.7%
6	Sodium acetate(50 mL)	75.2%
7	Sodium citrate(50 mL)	73.2%

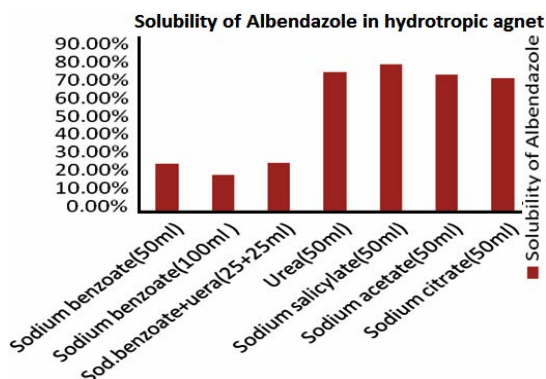


Fig. 2. Solubility of Albendazole with hydrotropic agent

CONCLUSION

As solubility of poor soluble drugs is a big concern, in this study an effort has been made to achieve maximum possible solubility of Albendazole by using different hydrotropic agents. Practical approach reveals that, various hydrotropic agents when added to water, they shows an enhancement

in solubility of Albendazole when added to the same. Among Sodium benzoate, Sodium salicylate, Urea, Sodium acetate and Sodium citrate solution, 1M Sodium salicylate in distilled water (50 mL) improve solubility of Albendazole, up to 80.7%. Sodium salicylate has an aromatic ring with an electron donating Hydroxyl group may be responsible for increase in solubility as well as drug release of Albendazole up to 80.7%.

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Conflicts of interest

The authors declare no conflict of interest.

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