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FORMULATION AND EVALUATION OF SELENIUM NANOPARTICLES OF ALBENDAZOLE FOR ORAL DELIVERY

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ABSTRACT

Selenium is an essential micronutrient required for proper functioning of biological and metabolic mechanism within the human body. Deficiency of selenium leads to the generation of several harmful disorders such as cancer, neurological, muscular, immune, *etc.* Albendazole is widely used to treat a variety of infections due to its high efficacy compared with others drugs; however, their side effects must be considered. The objective of the present study was to formulate and evaluate Selenium nanoparticles of Albendazole for oral delivery. SeNPs were synthesized by mixing the Albendazole drug with a salt stock solution. From all the formulations, formulation 4 was considered as the optimized formulation with 149.1 nm of particle size and -3.9mV zeta potential. The spectrum of UV–visible of the Albendazole shows an absorption peak at 291 nm due to the excitation of surface plasmon resonance (SPR). SEM image showed SeNPs have a spherical shape. The drug release data of selected batch were fitted into different kinetic models which show that the drug release from SeNPs follows Highuchi kinetic model. From the current research work it was concluded that the Albendazole loaded SeNPs consisting of better drug release and good stability.

KEYWORDS: Selenium, Albendazole, SeNPs, Highuchi kinetic model, Disorders.

1. INTRODUCTION

Nanotechnology is the science of the small; the very small. It is the use and manipulation of matter at a tiny scale. At this size, atoms and molecules work differently, and provide a variety of surprising and interesting uses. Nanotechnology and Nanoscience studies have emerged rapidly during the past years in a broad range of product domains. It provides

opportunities for the development of materials, including those for medical applications, where conventional techniques may reach their limits.[1,2] The oral route is also of interest for physiological reasons. The gastrointestinal (GI) tract offers extensive surface area (300–400 m^2) for drug absorption by absorptive epithelial cells (enterocytes).[3] The GI tract contains many other types of cells that may participate in drug absorption, including mucin-secreting goblet cells, endocrine cells, Paneth cells and specialized M cells associated with Peyer's patches that are responsible for antigen transportation through dendritic cells.[4] Numerous studies have shown that nanoparticles can improve the oral bioavailability of hydrophobic, hydrophilic and biologic drugs via various mechanisms. In fact, several oral nanosuspension-based products that improve drug dissolution and absorption are on the market.[5] Elemental selenium (Se) has great importance in the fields of physics, chemistry, and biology. Naturally, selenium exists in two forms: inorganic (selenite and selenate) and organic (selenomethionine and selenocysteine). Selenium is found in the form of both crystalline and amorphous polymorphic structures in nature. The bactericidal activity of selenium is because of its capacity to catalyse the oxidation of intracellular thiols, causing death of microscopic organisms.[6,7] The absorption profile of selenium indicates that nano-selenium can lead to a blue shift in the absorption spectrum and the range of this shift can vary from preparation to preparation. Thus, it is deduced that the bandgap of Se increases from 1.7 eV in bulk to 3.3 eV in the nano-range. The least toxic form of selenium is elemental Se, and hence its nano-form has attracted significant attention. Interestingly, functionalized SeNPs exhibit less cytotoxicity than their other forms such as selenate, selenite, selenoproteins, and inorganic selenium.[7] The biomedical applications of SeNPs have attracted global interest of many researchers due to their importance at cellular and tissue levels. It is well known that excessive production of toxic reactive oxygen species (ROS) can be triggered by various abiotic stresses, thus causing several diseases, due to damaged essential nutrients such as carbohydrates, proteins, and lipids.

Albendazole is an Anthelmintic agent, is mainly used in the management of Helminthiasis. It has biological half-life of up to 8.5 hrs. It is poorly absorbed from the gastrointestinal tract due to low aqueous solubility. An appropriately designed Novel Drug Delivery System can be a major advance for solving the problems related towards the release of the drug at specific site with specific rate. The need for delivering drugs to patients efficiently and with fewer side effects has prompted pharmaceutical companies to engage in the development of

new drug delivery system. Hence, the aim of this research work is to formulate and characterize the Albendazole loaded Selenium nanoparticles for oral delivery of bioactives.

2. MATERIALS AND METHODS

2.1 Materials

Sodium selenite was purchased from Sigma-Aldrich. Albendazole was gift sample. Acetone, Dichloromethane and Ethanol was purchased from Merck India Ltd. Mumbai, India. Demineralized and double distilled water was prepared freshly and used whenever required. All other reagents and chemicals used were of analytical grade.

2.2 Fourier transmission Infra-Red Spectroscopy

FT-IR spectrum of Drug was recorded over the range of 4000 to 400 cm−1 by KBr pellet method using a FT-IR spectrophotometer.[8]

2.3 Formulation of Selenium nanoparticle

SeNPs were synthesized by mixing the Albendazole drug with a salt stock solution. The stock solutions of sodium selenite (10 mM) were prepared by adding 1.25 g of sodium selenite salt to 500 mL of distilled water and then allowed to heat at 80 ◦C along with magnetic stirring on a hot plate for 30 min. Then, Different concentration (50, 100, 150, 200, 250 mg) of drug (Albendazole) was added drop wise into the stock solution until its color changed from green to brick-red after 1 to 2 h of continuous heating and magnetic stirring. When the brick-red color formed, it was then allowed to cool. Centrifugation was performed using a centrifuge machine at 1000 rpm for 15 min at 25 ◦C. The supernatant was discarded, and the pellet was collected by adding methanol. After it was collected, the pellet was centrifuged thrice to remove remaining drug and salt. The resulting selenium nanoparticles were subjected to characterization and then were used for in vitro purposes.[9]

Table 1: Composition of Selenium nanoparticle formulation.

S. no.	Drug concentration (mg)	Sodium Selenite (10 mM) (ml)	Stirring (time)
1	50	10.0	15
2	100	10.0	15
3	150	10.0	15
4	200	10.0	15
5	250	10.0	15

2.4 Characterization of Selenium nanoparticle

2.4.1 Particle size

The size of nanoparticle was measured using Malvern Zeta sizer (Malvern Instruments).[10]

2.4.2 Zeta potential

Zeta potential is analyzed by Zetasizer Malvern instruments.[11]

2.4.3 Entrapment efficiency

%Entrapment efficiency was determined by indirect estimation. Drug -loaded nanoparticles were centrifuged at 15,000 rpm for 30 min using REMI Ultra Centrifuge.

Entrapment efficiency % = Total drug conc. - Supernatant drug conc. / total drug conc.*100

2.4.5 Scanning Electron Microscopic (SEM)

The electron beam from a scanning electron microscope was used to attain the morphological features of the optimized nanoparticle were coated with a thin layer (2–20 nm) of metal(s) such as gold, palladium, or platinum using a sputter coater under vacuum.[12]

2.4.6 In-vitro drug release

To analyze the *in vitro* release data various kinetic models were use to describe the release kinetics. Zero - order kinetic model – Cumulative % drug released versus time. First – order kinetic model – Log cumulative percent drug remaining versus time. Higuchi's model – Cumulative percent drug released versus square root of time. Korsmeyer-Peppas model -- log cumulative % drug release vs log time (Korsmeyer–Peppas model).

3. RESULT AND DISCUSSION

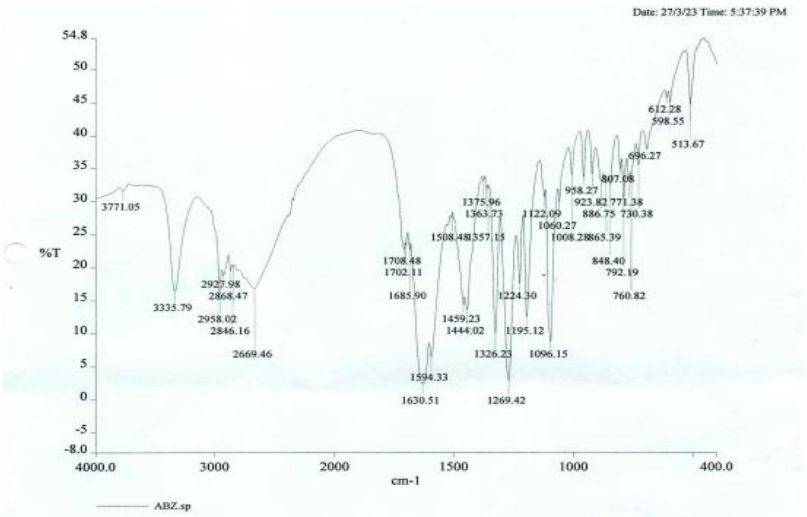

Figure 1: FTIR of Albendazole.

		Size (d.n...	% Number:	St Dev (d.n...
Z-Average (d.nm): 220.97	Peak 1:	246.5	100.0	15.8
PdI: 0.261	Peak 2:	0.000	0.0	0.000
Intercept: 0.896	Peak 3:	0.000	0.0	0.000
Result quality Good				

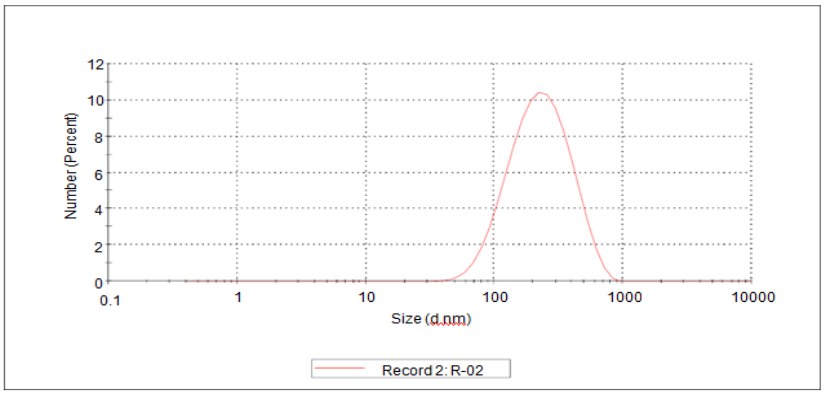

Figure 2: Particle size (Formulation 4).

DISCUSSION

Particle size analysis showed that the average particle size of nanoparticles was found to be range between 149.1 to 552.2 nm.

Zeta Potential (Mean) : -3.9 mV
Electrophoretic Mobility Mean : -0.000030 cm²/Vs

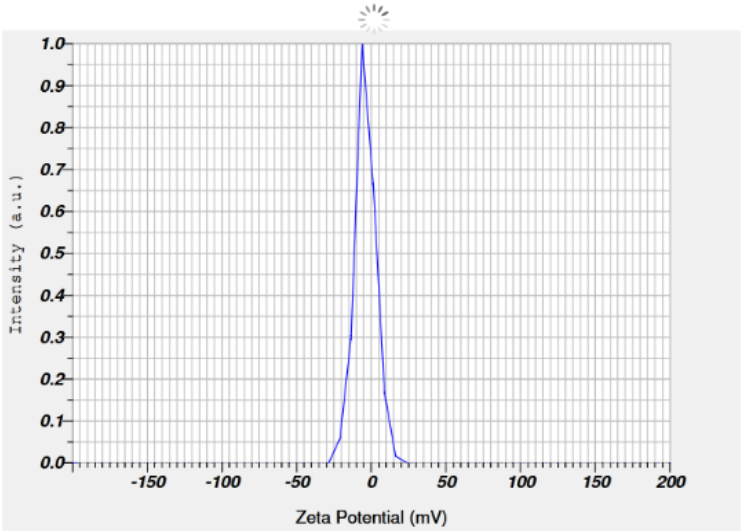

Figure 3: Zeta potential (Formulation 4).

Discussion

Zeta potential was found to be all formulation range -1.2 to -11.7 mV with peak area of 100% intensity. Zeta potential of Formulation 4 was -3.9 mV.

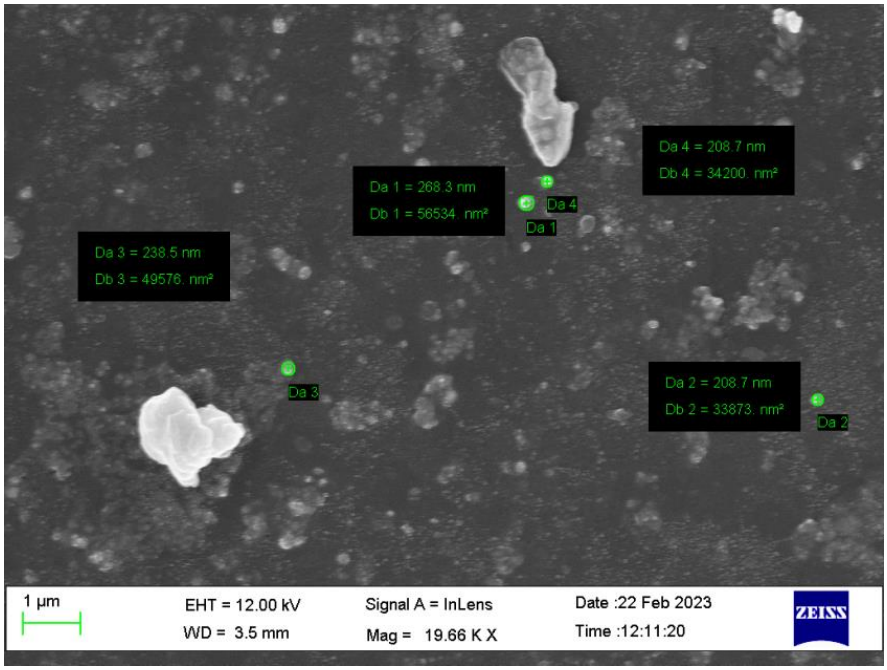

Figure 4: SEM (Formulation 4).

Discussion

Selenium nanoparticle were prepared and dried well to remove the moisture content and images were taken using scanning electron microscopy. Scanning electron micrograph of the prepared nanoparticle at 19.66 kx magnification showed that the nanoparticle were smooth surface morphology and spherical shape.

Table 2: Correlation value (R^2 value).

Formulation	Model	Kinetic parameter values
Nanoparticle	Zero Order	R^2 = 0.876
	First Order	R^2 = 0.887
	Higuchi	R^2 = 0.976
	Korsmeyer peppas	R^2 = 0.796

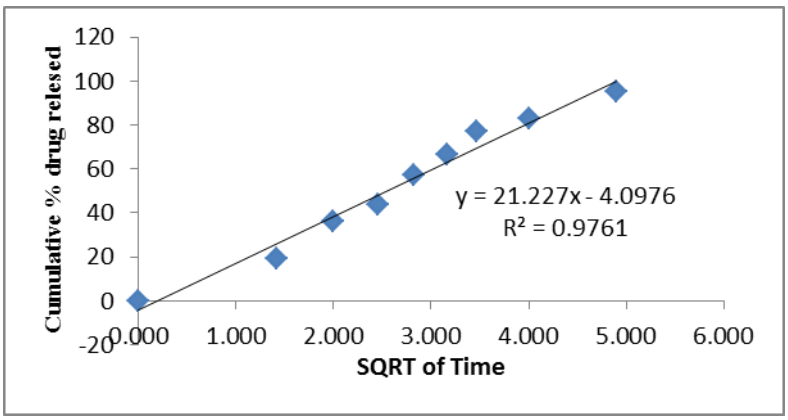

Figure 5: Higuchi model.

Discussion

The zero order graph of optimized formulation showed the constant drug release from the nanoparticle, the results of the zero order model was found to be $y = 3.896x + 17.52$ $R^2 = 0.876$. The results of first order kinetic model was found to be $y = -0.139x + 2.242$ $R^2 = 0.887$. The Higuchi model is used to describe the limits for transport and drug release. The Higuchi model of formulation was found to be, $y = 21.22x - 4.097$ $R^2 = 0.976$. And the results of Korsmeyer peppas kinetic model was found to be $y = 1.245x + 0.535$ $R^2 = 0.796$. *In-vitro* drug diffusion studies were carried out using dialysis bag method. On the basis of best fit with the highest correlation (R2) value it is concluded that in the optimized formulation of nanoparticles follow the Highuchi kinetic model.

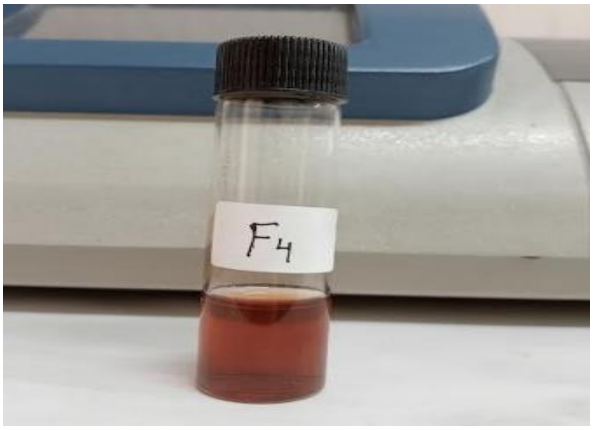

Figure 6: Visible observation of synthesized nanoparticle.

5. CONCLUSION

The authors concluded from the literature that mostly SeNPs ranging from 50 to 200 nm were effective for their use as a therapeutic agent in cancer treatment and antioxidant and antimicrobial applications. Albendazole is widely used to treat a variety of infections due to its high efficacy compared with others drugs; however, their side effects must be considered. Genotoxicity and neurotoxicity studies on humans should be done to clarify the role of Albendazole in human health. So this study focuses on the formulation and evaluation of selenium nanoparticle of Albendazole.

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