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LIST OF PUBLICATIONS

Research Articles

1. **Neha Rawat,** S. K. Singh, Ashish Baldi, Development and characterization of enteric polymer-based solid dispersion for cholecalciferol delivery. **Letters in Drug Design & Discovery,** 2024, 21, 918-927 (SCI Journal; Impact Factor 1.099).

2. **Neha Rawat**, Nabab Khan, S. K. Singh, U. K. Patil, Ashish Baldi**,** Delayed release HPMC capsules for efficient delivery of cholecalciferol solid dispersion. **Indian Journal of Pharmaceutical Education & Research** 2023, 57(2), 408-417 (SCI Journal, Impact Factor 0.97).

Review Articles

1 Gourav Paudwal[#], **Neha Rawat**[#], Gupta R, GD Singh, Ashish Baldi, PN Gupta, Recent advances in solid dispersion technology for efficient delivery of poorly water-soluble drugs, **Current Pharmaceutical Design,** 2019, 25, 1524-1535 (SCI Journal, Impact factor: 3.310; [#]Equal contribution).

2 Rahul Gupta, Chittaranjan Behera, Gourav Paudwal, **Neha Rawat**, Ashish Baldi, PN Gupta, Recent advances in formulation strategies for efficient delivery of vitamin D, **AAPS PharmSciTech**, 2019, 20(1),11 (SCI Journal, Impact Factor 4.026).

LIST OF PAPERS PRESENTED IN CONFERENCE/SEMINAR

1. Neha Rawat, Ashish Baldi, "Development of polymeric formulation for the efficient delivery of cholecalciferol", International seminar on "Current Trends in Chemical and Pharmaceutical Sciences" on 20-22 January 2021, organized by Dr. Harisingh Gour Vishwavidyalaya, Sagar, Madhya Pradesh.

2. Neha Rawat, Ashish Baldi, "Development of solid dispersion-based formulation for the delivery of cholecalciferol", International conference on "Current research trends in pharmacy, engineering, agriculture science, technology and management during pandemic" organized by Swami Vivekananda University, Sagar, Madhya Pradesh on 27-28 Feb 2021.

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RESEARCH ARTICLE

Development and Characterization of Enteric Polymer-based Solid Dispersion for Cholecalciferol Delivery

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Abstract: ***Background*:** The deficiency of vitamin D is a global concern affecting individuals of all age groups. Insufficient exposure to sunlight and disease conditions can lead to cholecalciferol (vitamin D3) deficiency.

***Objective*:** Cholecalciferol is a lipophilic crystalline molecule, and it is highly susceptible to degradation under environmental conditions, including light, temperature, and oxygen, and its degradation rate is high in the low pH range. Therefore, an enteric solid dispersion-based formulation was developed in the present study for the oral delivery of cholecalciferol.

***Methods*:** Enteric polymer hydroxypropylmethylcellulose acetate succinate (HPMCAS)-based solid dispersion was developed and characterized by Fourier transform-infrared spectroscopy (FTIR), differential scanning calorimetry (DSC), scanning electron microscopy (SEM), and X-ray diffraction analysis. The effect of various concentrations of cholecalciferol formulations on the viability of Caco-2 cells was determined using an MTT assay. A dissolution and stability study of the product was also performed.

***Results*:** An amorphous form of cholecalciferol in the solid dispersion was reported. The drug content of solid dispersions was in the order of 90%. The viability assay indicated that the surfactant used in the developed solid dispersion of cholecalciferol had no cytotoxic effect on Caco-2 cells. A dissolution study on enteric solid dispersion in two-stage dissolution under a biomimetic medium indicated the pH-dependent release of cholecalciferol from the HPMCAS-based solid dispersion. Moreover, the stability study showed no significant changes in the cholecalciferol content in the developed formulation under storage at experimental conditions.

***Conclusion*:** The enteric solid dispersion of cholecalciferol was developed, which exhibited compatibility with Caco-2 cells, improved dissolution, and acceptable stability profile, and represented a potential option for efficient delivery of cholecalciferol.

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1. INTRODUCTION

Vitamin D has been recognized as an essential nutrient for bone health, and its deficiency is a global concern [1]. As per the International Osteoporosis Foundation report, in the northern part of India, vitamin D deficiency is widespread, affecting neonates (96%), healthy hospital staff (78%), healthy school girls (91%), and pregnant women (84%), while in the southern part of India, vitamin D deficiency was found in 40% of males and 70% of females [2]. In another investigation conducted in Europe on women over 80 years of age, the level of vitamin D deficiency was observed to be 80.9% [3]. This deficiency is common in both rural and urban areas affecting people of all socioeconomic and geographical groups [4]. Reduced exposure to sunlight is the main reason for its deficiency, as ultraviolet-B exposure of 7-dehydrocholesterol in skin epidermal cells is the main source of vitamin D [5]. Vitamin D is an essential micronutrient owing to its ability to maintain calcium and phosphorus concentrations at the required level by improving the efficacy of the small intestine to absorb these minerals from the diet. The deficiency of vitamin D leads to rickets, osteomalacia, hyperparathyroidism, and osteoporosis [6, 7]. Cardiovascular mortality has also been reported in type 2 diabetes mellitus patients with vitamin D deficiency [8]. The regu-

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Original Article

Delayed Release HPMC Capsules for Efficient Delivery of Cholecalciferol Solid Dispersion

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ABSTRACT

Introduction: The deficiency of Vitamin D is associated with an increased risk of various diseases and deficiency of this Vitamin is recognized in individuals all over the world. Therefore, the intake of Vitamin D has become essential. **Objectives:** Cholecalciferol (Vitamin D_3) is a poorly soluble molecule and it is very sensitive to degradation under environmental factors such as light, temperature, and oxygen. Its stability is also affected adversely under acidic conditions. Therefore, solid dispersion-based formulation for cholecalciferol was developed and encapsulated in delayed release hydroxypropylmethyl cellulose (HPMC) capsules. **Materials and Methods:** Cholecalciferol solid dispersion was developed and characterized by Fourier transform–infra red spectroscopy (FTIR), differential scanning calorimetry (DSC), scanning electron microscopy (SEM), and X-ray diffraction analysis. The effect of various concentrations of cholecalciferol formulations on the viability of Caco-2 cells was determined by using MTT assay. Dissolution profile and stability study of the developed product was also evaluated. **Results:** The results demonstrated improved solubility of cholecalciferol in solid dispersion-based formulation. The drug content of solid dispersions was in the order of 91±2.3% and various studies showed the amorphous form of cholecalciferol in the solid dispersion. The cell viability assay in Caco-2 cells demonstrated that the surfactant used in the solid dispersion formulation of cholecalciferol had no adverse effect on intestinal cells. Further, dissolution profile of HPMC capsule encapsulated solid dispersion showed improved dissolution of cholecalciferol. Moreover, the stability study indicated no significant changes in the cholecalciferol content in the developed formulation under storage at experimental conditions. **Conclusion:** The solid dispersion-based formulation of cholecalciferol exhibited improved solubility and found to be compatible with Caco-2 cells. The delayed release HPMC capsule encapsulated solid dispersion of cholecalciferol (DRHCap-SD) showed improved dissolution and acceptable stability profile and this represent a potential delivery system for oral administration of cholecalciferol.

Keywords: Solid dispersion, Cholecalciferol, HPMC capsule, Caco-2 cells, Oral delivery, Dissolution.

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INTRODUCTION

The deficiency of Vitamin D is gaining immense recognition as a serious health concern leading to a variety of health issues.[1,2] This vitamin is synthesized in the skin following the exposure of sunlight or this micronutrient can also be obtained from food sources.[3] Food based options for this Vitamin is scanty and deficiency of Vitamin D has been recognized in many countries.[4,5] Limited exposure to the sunlight and sedentary lifestyle is the main factors associated with the deficiency of Vitamin D. The deficiency of Vitamin D is linked with an increased susceptibility towards many ailments such as diabetes, cancers, cognitive decline and depression.[1,2,6,7] Vitamin D is an essential micronutrient owing to its ability to maintain calcium and phosphorus concentrations at the desired level by improving the ability of the intestine to absorb calcium and phosphorus from the food sources. The Vitamin D deficiency leads to rickets, osteomalacia, hyperparathyroidism, and osteoporosis.[8,9] Cardiovascular mortality has also been reported in type 2 diabetes mellitus patients with Vitamin D deficiency.[10] The regular dose of Vitamin D (about 2000 IU/d) was reported to reduce the risk of developing type 1 diabetes as its low levels are associated with insulinemia and glucose intolerance.[11] The potential of Vitamin D derivatives as an antitumor molecule has been documented owing to their property of hampering angiogenesis.[12] Keeping all these aspects into considerations, the intake of Vitamin D has become essential.

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