

Stability Testing of Non-Toxic Bismuth Vanadate According to Pharmaceutical Criteria

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ABSTRACT: Bismuth vanadate is high performance inorganic pigment. Its LD₅₀ cut off value is more than 5000 mg/kg body weight of rat. Thus it is acute oral nontoxic pigment. In addition to non-toxicity the property of thermal stability has helped the pigment to replace toxic cadmium and lead-based pigments in paints. It is also a pigment of choice for plastic industry. BiVO₄ finds applications in cosmetics formulations. Also it is considered to be an excellent photocatalyst. However, the state of art is silent with its application in pharmaceutical sector. In our research an attempt is made to introduce thermally stable, non toxic BiVO₄ for pharmaceutical formulations. The scope of present literature is restricted to the stability testing of BiVO₄ as per pharmaceutical criterion.

BiVO₄ synthesised by improved solid state route was selected for chemical stress and photo-radiations sustainability study. The pre and post degradation study was evaluated on the basis of FT-IR study.

KEYWORDS: BiVO₄, chemical stress testing, photo- radiations sustainability study.

I. INTRODUCTION

The colourants work as cosmetics for the pharmaceutical formulations. Therefore, selection of appropriate colourant for a specific pharmaceutical dosage form plays an important role in manufacturing of the pharmaceutical dosage forms [1]. Colourants are subdivided into dyes (water-soluble substances), lakes (insoluble forms of a dye resulting from its irreversible adsorption onto a hydrous metal oxide), inorganic pigments (substances such as titanium dioxide or iron oxides) and natural colourants (coloured compounds which are not considered as dyes e.g. riboflavin) [2].

Selection of pharmaceutical colouring agent is depended on its physical and chemical properties. Particle size and size distribution of dyes and lakes can influence product processing times (blending and dissolution), colour intensity and uniformity of appearance.

The most important properties of a colouring agent are its depth of colour and resistance to fading over time. Substances can be graded on their efficiency in reflecting desired colours of visible light, as well as on their molar absorptivity at characteristic wavelengths of absorbance. Obviously, the substance should be physically and chemically non-reactive with formulation ingredients and drug substances. The quality of a colouring agent is ordinarily measured by determination of its strength, performance or assay.

Inorganic pigments when used in tablet coatings or gelatin shells, due to their opacity and light fastness properties, protect active pharmaceutical agents from light radiations, contamination and thus also provide different identification [3]. Additionally, inorganic pigments and lakes are of low hazard, but it requires standard chemical handling precautions depending upon the circumstances and quantity of material handled. Special attention needs to be given to prevent excessive dust generation and thus to avoid inhalation problems [4].

Main pigments such as the iron oxides, titanium dioxide and few aluminium lakes are existing colourants for medicinal purposes. However, all the existing colourants have various limitations in concern to synthesis and application in

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pharmaceutical range. Therefore, a compound is very much required which will be physico-chemically stable to external environmental conditions and also economical to synthesis.

The patent US 7485183 B2 granted in 2009 and US Patent application published in recent years US 2008/0274198 A1, US 2009/0246294 A1 and US 2011/0300200 A1 describe about the processing and use of existing pigments in food, cosmetics and pharmaceutical areas. However, the state of art is silent about the application of nontoxic pigment bismuth vanadates (BiVO_4) in pharmaceutical formulation especially in solid dosage form as a colourant.

BiVO_4 , C. I. Pigment Yellow 184, is a pigment possessing a greenish yellow colour, having high tinting strength, high chroma and very good hiding power. In short it is a high performance inorganic pigment that can eliminate the more expensive and less stable organic pigments. It is classified as nontoxic and has proved to be a replacement for toxic inorganic pigments such as cadmium and lead-based paints. In addition to thermal stability, it is also considered having superlative fastness to weathering [5,6]. BiVO_4 pigments are not acute toxic for either on inhalation or oral incorporation [6]. Its LD_{50} cut off value is more than 5000 mg/kg body weight of rat [5].

In our article [7] we have proposed an improved solid state route for the synthesis of thermally stable BiVO_4 . The calculated density of BiVO_4 synthesised by improved solid state route is 6.94 [7] which matches with the literature value [5]. Compared to pharmaceutically accepted pigment yellow iron oxide, BiVO_4 is a high density colourant. The use of high density pigment in pharmaceutical formulations may eliminate the inhalation problem occurring due to dust generation. Accordingly, BiVO_4 may serve as a better alternative to yellow iron oxide for pharmaceutical formulations.

From an application point of view, bismuth vanadate was claimed to impart light fastness to paints in 1978 (US 4115142). Patent US 5203917 claims about the colouring application of tetragonal BiVO_4 in plastic and resin. In 2002, L'Oreal (US 6203807) proposed a coloured composition for the dermal (topical) application, which comprises hydrophilic continuous phase bismuth vanadate as a colouring agent. It also claims about a method for the cosmetic protection of the skin against the harmful effect of free radicals. Application of BiVO_4 photocatalyst as a bleaching agent in tooth paste has been proposed in patent EP1669059 A1 in 2005. Photocatalytic activity of bismuth vanadate for degradation of organic materials especially organic dyes has been studied by many researchers [8-19]. It is also a colourant of choice for food contact plastics [20]. Through our research an attempt is made to introduce nontoxic BiVO_4 to pharmaceutical sector. The scope of present literature is restricted to the stability testing of BiVO_4 as per pharmaceutical criterion.

Stress testing study

Stability plays an important role in the drug development process. It explains several factors that affect the expiry date of drug products, including the chemical and physical stability during the pre-clinical formulation stages, process development, packaging development and post-marketing life. The evaluation of the physicochemical stability of a given product requires an understanding of the physical and chemical properties of the drug substance. Lack of drug substance or drug product stability may affect the purity, potency and safety of the drug product. Pharmaceutical stability may be applied in several ways. Therefore, the performance of a drug will be evaluated depending on whether it assesses a drug substance, a formulation, a drug product or a packaged product [21]. The same rule is applicable for excipient, even for colouring agent.

The study has been formulated to check the stability of synthesised pigment under the influence of chemical stress conditions [22] and photo-radiations [23].

II. MATERIALS AND METHOD

Materials

Stability testing study was carried out on BiVO_4 synthesised by improved solid state route. All the chemicals used were of AR grade and used as received from Merck India, without further purification. Deionised water was used where required. The details about the BiVO_4 synthesis process and its characterisation are available in literature [7].

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Chemical stress study

The chemical stress testing study of the synthesised pigment BiVO_4 was carried out in three different conditions viz. acidic, basic and oxidising medium. For these, a known quantity of dried BiVO_4 was treated with 0.1N HCl ($\text{pH}=2.0\pm 0.2$), 0.1N NaOH ($\text{pH}=10.0\pm 0.2$) and 3% of H_2O_2 (neutral) for more than 10 days continuously at room temperature and pressure, in absence of light. Treated compound was filtered with sintered glass crucible and washed by deionized water followed by drying at 100°C for 24 hours. The dried compound was evaluated by FT-IR analysis for chemical transformation, if any.

Photostability study

Evenly spread thin layer of synthesized BiVO_4 pigment was exposed to solar irradiations for 50 hours and evaluated through FT-IR analysis for any alteration.

III. RESULTS AND DISCUSSION

The effect of stress condition on BiVO_4 about chemical degradation can be observed from Fig. 1. Examining degradation products under stress conditions is useful in establishing degradation pathways and developing and validating suitable analytical procedures.

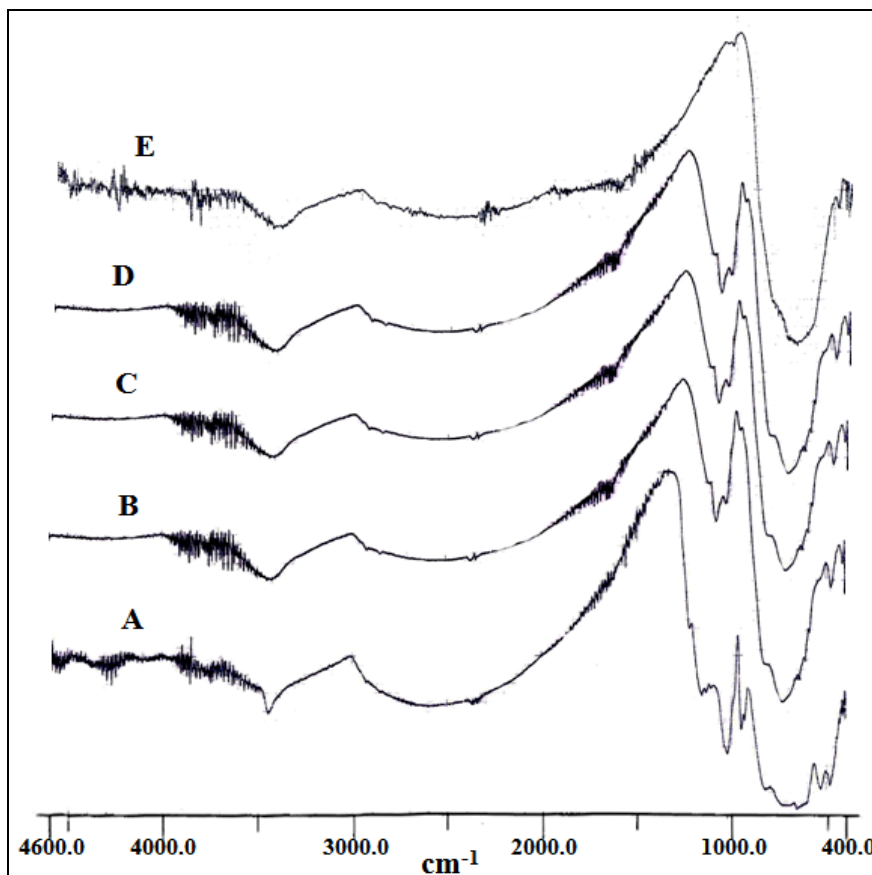


Fig. 1. FT-IR spectra for stability testing study of bismuth vanadate (BiVO_4)

- (A) BiVO_4
- (B) Stress testing of BiVO_4 in 0.1N HCl
- (C) Stress testing of BiVO_4 in 0.1N NaOH
- (D) Stress testing of BiVO_4 in 3% H_2O_2
- (E) Photo-radiations effect on BiVO_4

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All the possible V–O and Bi–O bands which are depicted for controlled BiVO₄ (Fig. 1.(A)) are clearly seen in Fig. 1.(B), 1.(C) and 1.(D). Eliminating the peak around 3400 cm⁻¹ which is possibly due to moisture in air, other expected bands are indistinctly observed in Fig. 1.(B), (C) and (D). This indicates that the synthesised BiVO₄ can sustain the specified stress conditions.

Considering the direct exposure of BiVO₄ to solar radiations, Fig. 1.(E) records a distinct change in dipole moments of BiVO₄ resulting in the change in intensity of band at around 1010 cm⁻¹, but the possible V–O and Bi–O bonds below 900 cm⁻¹ has remained unchanged even when exposed to strong solar radiations. This explains the capability of BiVO₄ to sustain the solar radiations.

Investigated results of FT-IR show that there were no alterations or degradations observed in chemical stress tested BiVO₄ and photo-radiation exposed BiVO₄, which indicates that it has ability to withstand against the specified conditions.

IV. CONCLUSION

The stability study has been successfully applied for synthesised BiVO₄. It can be concluded that pigment possesses the property to withstand the chemical stress conditions as well as solar radiation effect. Thus, synthesised pigment proves its potential under a variety of ICH recommended conditions. Therefore, this nontoxic, thermally stable pigment can be employed as a subsidiary pharmaceutical colouring agent.

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BIOGRAPHY



Harshada D. Telpande is M. Sc. in Chemistry of Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur. She has submitted her thesis for the award of Ph. D. degree to the same University. Her current area of research includes synthesis, characterization and application studies of inorganic pigments. She has also studied the effect of gamma radiations on synthesized pigment.



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