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2021	10		
2020	15		
2019	04		
2018	04		
2017	01		







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Title of paper	Name of the author/s	Department of the teacher	Name of journal	Year of publication		Link to the recognition in UGC enlistment of the Journal /Digital Object Identifier		
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Research Article

SYNTHESIS AND CHARECTERIZATION OF DIPYRIDAMOLE IMPURITIES BY SEQUENTIAL NUCLEOPHYLLIC SUBSTITUTION REACTION

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ABSTRACT

Dipyridamole is used as drug for the treatment to inhibits blood clot formation and causes blood vessel dilation when given at high doses over a short time by inhibiting the phosphodiesterase enzymes that normally break down cAMP by increasing cellular cAMP levels and blocking the platelet aggregation response to ADP and cGMP. Presence of higher level of related substances or impurities may have harmful effect on body, hence needed to be identified, synthesised &characterised for safer use of the medicine. During process optimization of Dipyridamole drug, impurities were observed. These related substances or impurities were synthesised, characterized and proposed structures we reconfirmed by chemical synthesis. Dipyridamole impurities containing pyrimido-pyrimidine have been synthesized by the reaction of 2,4,6,8-tetrachloropyrimido[5,4-d] pyrimidine with sequential nucleophilic substitutions of piperidine, diethanolamine and ethanolamine in the pattern of C-4, C-8, C-2 and C-6 respectively. Which have been characterized by using LCMS, ¹H NMR and HPLC analysis.

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INTRODUCTION

Dipyridamole is used as drug for the treatment to inhibits blood clot formation, It is used to dilate blood vessels (Boehringer Ingelheim Pharmaceuticals, Inc. 2016) in people with peripheral arterial disease and coronary artery disease and it has been shown to lower pulmonary hypertension without significant drop of systemic blood pressure (Brown DG et al, 2015; Dixon BS et al 2009; Derendorf H et al, 2005). The safety of a drug product is not only dependent on the toxicological properties of the active drug substance or API (De Schryver EL et al, 2007; Sprigg N et al, 2008), but also on the impurities formed during the various chemical transformations. Therefore, identification, quantification, and control of impurities in the drug substance and drug product are important parts of drug development for obtaining marketing approval (S.J. Ingale et al, 2011; Brown D.G et al, 2015). As per the guidelines recommended by ICH, the acceptable level for a known or Unknown impurity or related substances is less than 0.2% in a drug substance. Tomeet the stringent regulatory requirements, it is more challenging for pharma industry to identify the impurities which are formed in very small quantities in a drug substance. Since most of the time it is very difficult to identify and control impurities within acceptable levels in the process, extra purification steps may then be necessary thereby making the process less competitive (V.S. Tegeli et al, 2011; B. Misralet al, 2015). The syntheses of impurities are not described in the literature which makes it even more difficult for the organic chemist who must then design a synthesis, which is time consuming. The development of a drug substance is incomplete without the identification of an impurity profile involved in the process. In our study we explored the identification, synthesis and characterization of impurities found in the preparation of dipyridamole. This study will be of immense help for the pharma industry to understand the potential impurities in dipyridamole synthesis and thereby obtain the pure compound (FA Attaby et al. 1995; SS Ghabrial et al, 1996; S Ranjit Pada et al, 2012). The object of this invention to provide novel synthetic route with high purity of dipyridamole impurities containing pyrimidopyrimidine nucleus, upon further study of the specification and appended claims, Pyrimidopyrimidines have been drawn as promising structural units in the field of medicinal chemistry. Pyrimido-pyrimidine derivatives exhibit various types of physiological activity and enter medicinal products and this determines the great attention that has been paid to the synthesis of new compounds of this series. The pyrimido-pyrimidine derivatives drew a lot of attention on various pharmacological activities because of their structural similarity to Purines, like anti-

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