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RESEARCH ARTICLE

STABILITY INDICATING ASSAY METHOD DEVELOPMENT AND VALIDATION OF DRONEDARONE HYDROCHLORIDE IN ITS BULK FORM BY RP-HPLC

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This study describes the development and validation of stability indicating HPLC method for dronedarone hydrochloride in its bulk form. Dronedarone was subjected to stress degradation under different conditions recommended by International Conference on Harmonization. The sample so generated was used to develop a stability indicating high performance liquid chromatographic method for dronedarone·HCl. The peak for dronedarone·HCl was well resolved from the peaks of degradation products, using a kromasil C18 (250 mm × 4.6 mm, 5 μm) column and mobile phase comprising of buffer:methanol (buffer:30 mM KH_2PO_4 + 1 ml triethylamine in 1 litre water, pH=3.6 adjusted with ortho-phosphoric acid) using the gradient method at a flow rate of 1 ml/min. Detection was carried out using a UV detector at 291 nm. The degradation product peak was well resolved from drug peak. The method proved to be specific to the drug and its degradation products. The developed HPLC method was validated with respect to linearity, accuracy, precision and robustness. All the results were found to be within the specification limit.

Key words: Dronedarone hydrochloride, HPLC, Validation, Forced degradation, Stability indicating.

INTRODUCTION

Dronedarone hydrochloride is a class III anti-arrhythmic drug that is mainly used for treatment of atrial fibrillation and atrial flutter of cardiac arrhythmia. Dronedarone is a benzofuran derivative and is chemically *N*-(2-Butyl-3-(4-(3-(dibutylamino)propoxy) benzoyl)-5-benzofuranyl)-methanesulfonamide (Mol. formula: $C_{31}H_{44}N_2O_5$·HCl, Mol. wt.: 556.76 g/mole) (**Figure 1**).

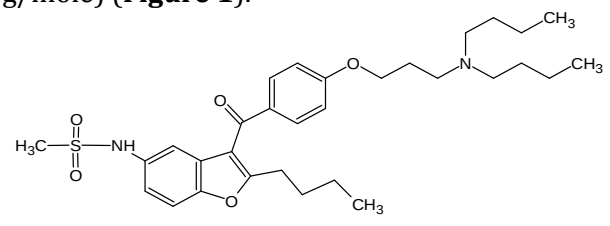

Fig. 1. Structure of dronedarone·HCl

Dronedarone is recommended as an alternative drug of amiodarone for treatment of atrial fibrillation and atrial flutter in cases where heart requires drug therapy or electric shock treatment to maintain normal rhythm of heart. Dronedarone is the most recent anti-arrhythmic drug (AAD) which is approved by USFDA and is available in the USA as Multaq tablets (400 mg). It mainly targets the repolarization currents, making them less active and hence prolonging the action potential duration (APD). Dronedarone also exhibits anti-adrenergic activity. Dronedarone is significantly safer and effective in maintaining the sinus rhythm and reducing the ventricular pro-arrhythmic, justifying it for the long term treatment of atrial fibrillation compared to other anti-arrhythmic drugs. HPLC is a well-known and widely used