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Development and Validation of a Stability-Indicating High Performance Liquid Chromatographic Method for the Determination of Domperidone in Bulk and Pharmaceutical Dosage Forms

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1. Introduction

In the present study a simple high performance liquid chromatography combined with ultraviolet detection was developed and validated for the determination of domperidone in bulk and tablet dosage forms using standard and stressed degradation samples. There is no monograph for finished product/bulk of domperidone in the United States Pharmacopeia 41. The British Pharmacopoeia (BP 2019) comments perchloric acid titration for assay of domperidone and domperidone maleate bulk forms. There is no information about the stability–indicating nature of those proposed methods. Therefore, in this work, forced degradation studies were carried out on bulk samples and tablet dosage forms of domperidone using acid, base, hydrogen peroxide, heat and ultraviolet light as described by ICH for stress conditions to develop and demonstrate the stability-indicating analytical method.

2. Materials and methods

Separation was achieved on a C18-ACE (5 µm, 150 mm x 4.6 mm i.d.) column using a mobile phase consisting of ammonium acetate buffer (5 g/L, pH=6.8)-acetonitrile-methanol (50:20:30 volumetric ratio) at a flow rate of 1 mL/min and ultraviolet detection at 230 nm. The separation was carried out at room temperature and the injection volume of 20 µL was used. The method selectivity was evaluated by peak purity test using a photo diode array detector. The calibration curve was found to be linear with the equation y=106945x-187069 and a linear regression coefficient (R) of 0.9987 over the concentration range 10–150 µg/mL.

3. Results

Typically the necessary stress conditions are determined on the basis of the experience of the analyst conducting the studies or by trial and error. The conditions used to effect degradation including the concentration of stress agent and time of exposure were obtained by experiments and degradations without complete destruction of DP were achieved. The best chromatographic separation was achieved on a C18–ACE® (5 µm, 150 mm x 4.6 mm i.d.) column using a mobile phase consisting of ammonium acetate buffer (5 g/L, pH=6.8)-acetonitrile-methanol (50:20:30 volumetric ratio) at a flow rate of 1 mL/min and ultraviolet detection at 230 nm. The column was maintained at laboratory temperature and an injection volume of 20 µL was used. Peak purity values were obtained using Alliance Waters 2695 HPLC system with Waters diode array detector (2996 PDA, Waters, USA). The results were analyzed by Empower PDA Software 1154. Based on the manual of Empower PDA Software, if the calculated Purity Angle is less than the Purity Threshold, the peak is spectrally homogeneous. For all samples (Table 1), Purity Angles were less than the Purity Thresholds, indicating that the peaks were homogenous, thereby establishing the selectivity of present method for tablets assay. Typical chromatograms were obtained following the assay of untreated tablet powder sample and stressed tablet samples are shown in ***Figure 1***.

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Table 1 *Purity Angle and Purity Threshold data obtained from Empower PDA Software for DP peaks*

Stress Conditions	Drug form	Purity Angle	Purity Threshold
0.1 M HCl	*Tablet*	*0.357*	*0.417*
	API	*0.336*	*0.454*
0.1 M NaOH	*Tablet*	*0.336*	*0.448*
	API	*0.328*	*0.464*
0.3% H_2O_2	*Tablet*	*0.357*	*0.483*
	API	*0.320*	*0.453*
UV Light (Solid)	*Tablet*	*0.366*	*0.412*
	API	*0.358*	*0.454*
UV Light (Solution)	*Tablet*	*0.374*	*0.398*
	API	*0.326*	*0.389*
Dry Heat, 70 °C	*Tablet*	*0.625*	*0.676*
	API	*0.692*	*0.753*
Neutral Hydrolysis	*Tablet*	*0.337*	*0.467*
	API	*0.399*	*0.423*
Untreated samples	*Tablet*	*0.369*	*0.444*
	API	*0.370*	*0.477*

4. Conclusions

In this study a stability–indicating HPLC method was developed, validated and applied for the assay of DP in bulk and tablet dosage forms. The results of stress tests on API and tablets indicate that the validated method is selective and stability-indicating. The proposed method is simple, precise, accurate, and has the ability to separate parent compound from its degradation products and excipients found in tablet dosage forms. In addition, the HPLC method can be applied to the analysis of samples obtained during stability studies and quality control process.

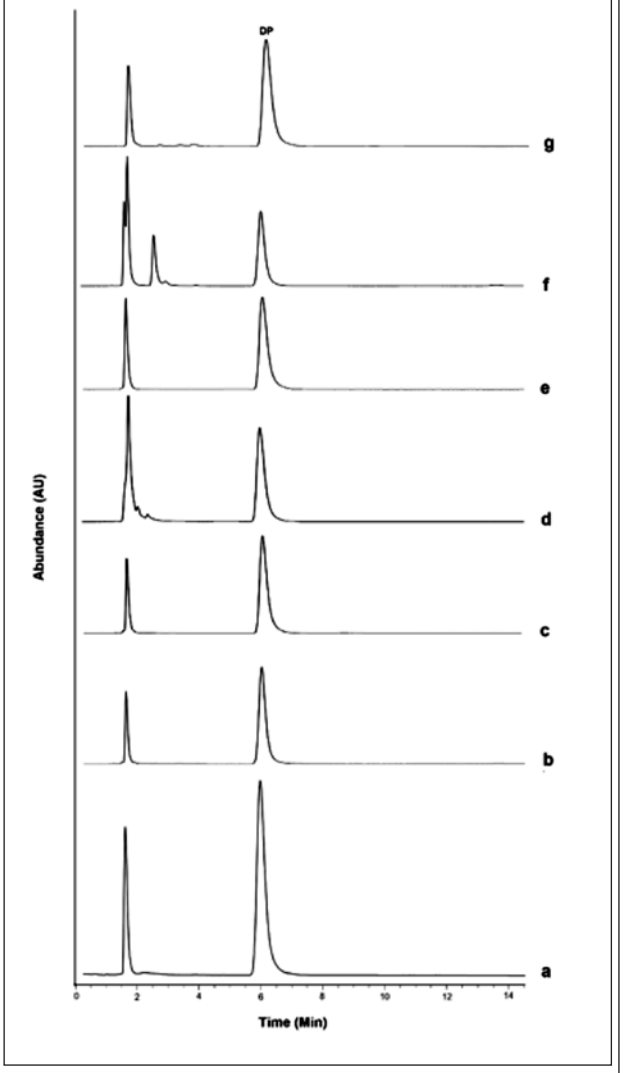

Figure 1 *Typical HPLC chromatograms obtained from analyses of domperidone (DP) tablets: (a) untreated sample, (b) photodegraded sample (solution); (c) photodegraded sample (solid); (d) base hydrolysis degraded sample; (e) acid hydrolysis degraded sample; (f) oxidative degraded sample; and (g) dry-heated sample.*

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