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ORIGINAL ARTICLE

Validated HPTLC methods for determination of some selected antihypertensive mixtures in their combined dosage forms

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Abstract Simple and selective HPTLC methods were developed for the simultaneous determination of the antihypertensive drugs; carvedilol and hydrochlorothiazide in their binary mixture (Mixture I) and amlodipine besylate, valsartan, and hydrochlorothiazide in their combined ternary formulation (Mixture II). Effective chromatographic separation was achieved on Fluka TLC plates 20 × 20 cm aluminum cards, 0.2 mm thickness through linear ascending development. For Mixture I, the mobile phase composed of chloroform–methanol in the ratio 8:2 v/v. Detection was performed at 254 nm for both carvedilol and hydrochlorothiazide. For Mixture II, the mobile phase was chloroform–methanol–ammonia in the volume ratio 8:2:0.1. Detection was performed at 254 nm for valsartan and hydrochlorothiazide, and at 365 nm for amlodipine. Quantification was based on spectrodensitometric analysis. Analytical performance of the proposed HPTLC procedures was statistically validated with respect to linearity, ranges, precision, accuracy, specificity, robustness, detection and quantification limits. The linearity ranges were 0.05–1.0 and 0.1–2.0 μg/spot for carvedilol and hydrochlorothiazide, respectively in Mixture I, 0.1–2.0, 0.1–2.0 and 0.2–4.0 μg/spot for amlodipine, hydrochlorothiazide and valsartan, respectively in Mixture II, with correlation coefficients > 0.9992. The validated HPTLC methods were applied to the analysis of the cited antihypertensive drugs in their combined pharmaceutical tablets. The proposed methods confirmed peak identity and purity.

1. Introduction

Carvedilol (CRV) (Fig. 1), chemically known as (2RS)-1-(9H-carbazol-4-yloxy)-3-[[2-(2-ethoxyphenoxy)ethyl]amino]propan-2-ol,[1] is a non-cardioselective beta blocker. It has vasodilating properties, which are attributed mainly to its alpha-1 blocking

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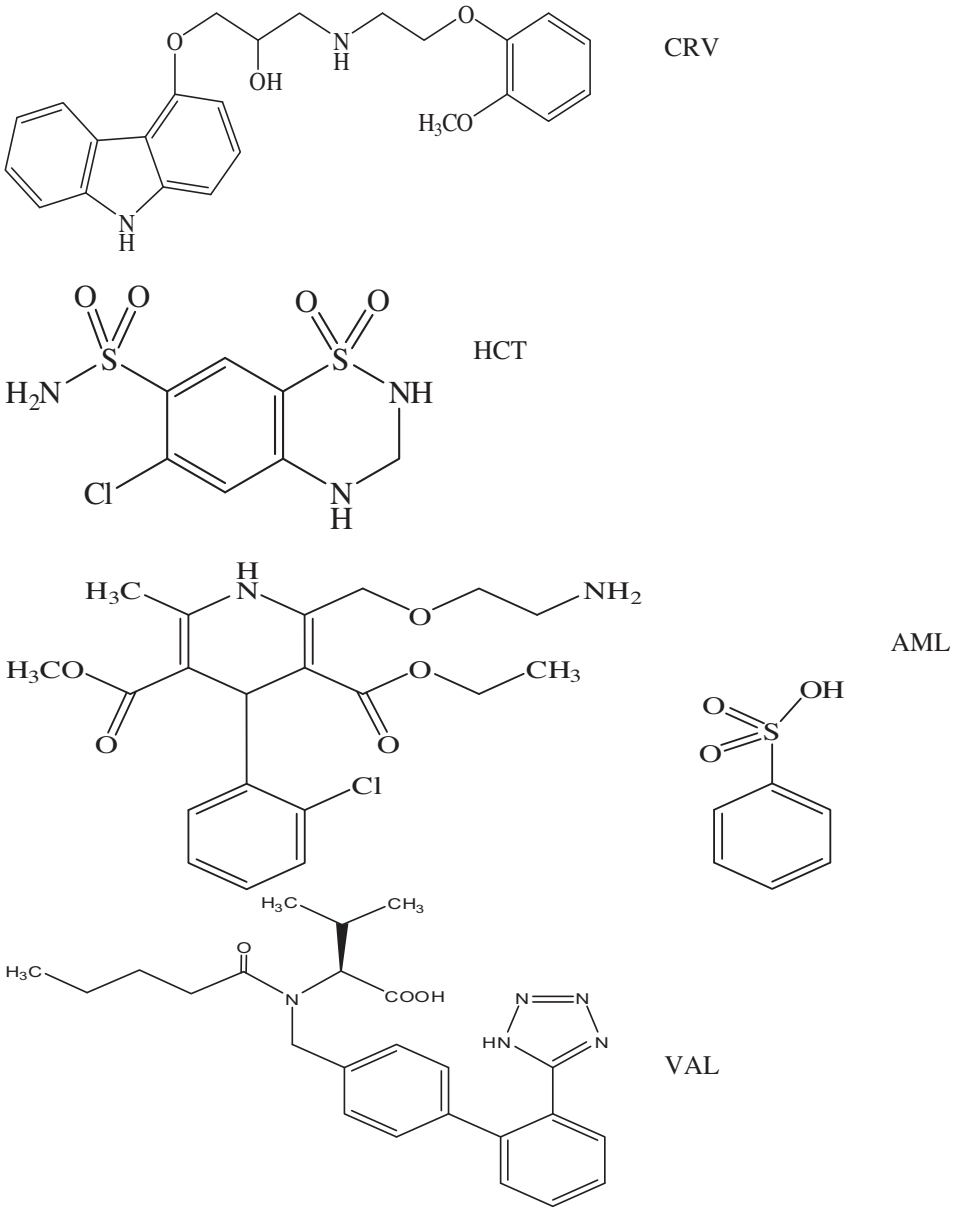

Figure 1 Chemical structures of carvedilol (CRV), hydrochlorothiazide (HCT), amlodipine besylate (AML) and valsartan (VAL).

activity; at higher doses, calcium channel blocking activity may contribute. CRV is used in the management of hypertension, angina pectoris and as an adjunct to standard therapy in symptomatic heart failure.[2] Hydrochlorothiazide (HCT) (Fig. 1), chemically known as 6-chloro-3,4-dihydro-2H-1,2,4-benzothiadiazine-7-sulfonamide-1,1-dioxide,[1] is a moderately potent diuretic. HCT is used in the treatment of hypertension either alone or with other antihypertensives. It is also used to treat edema associated with heart failure and with renal and hepatic disorders.[2] The fixed dose combination of CRV and HCT has been used for the treatment of essential hypertension particularly if with the monotherapy no sufficient blood pressure lowering can be achieved.[3] The simultaneous determination of CRV and HCT in their binary combination was addressed in few analytical reports. These reports proposed several spectrophotometric[4,5] and RP-HPLC with UV detection methods.[4,6] A stability-indicating HPLC method was recently published.[7] The fact that up till now the simultaneous HPTLC determination of this binary mixture has been reported in the literature in only one report[8] has encouraged us to develop this work.

Amlodipine besylate (AML) (Fig. 1), chemically known as 3-ethyl-5-methyl2-(2-aminoethoxymethyl)-4-(2-chlorophenyl)-1,4-dihydro-6-methylpyridine-3,5-dicarboxylate benzenesulphonate,[2] is a dihydropyridine calcium channel blocker used in the treatment of hypertension and angina pectoris.[2] Valsartan (VAL) (Fig. 1), chemically known as N-[p-(o-1H-tetrazol-5-ylphenyl)benzyl]-N-valeryl-L-valine,[2] is an angiotensin II receptor antagonist used in the management of hypertension, to reduce cardiovascular mortality in myocardial infarction patients and in the management of heart failure.[2] In 2009, the US Food and Drug Administration (FDA) and the European Medicines Agency approved a triple fixed-dose combination of AML, VAL and HCT. It was found that the use of this triple combination was generally more effective in reducing blood pressure and providing overall blood pressure