

Optimasi dan validasi metode bioanalisis kurkumin plasma manusia secara kromatografi cair kinerja ultra tinggi-tandem spektrometer massa (KCKUT-SM/SM) dan aplikasinya secara in vivo = Optimatization and validation bioanalytical method of curcumin in human plasma by ultra performace liquid chromatography mass spectrometry (UPCL-SM/MS and it s application to in vivo study

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Abstrak

[ABSTRAK

Kurkumin merupakan senyawa polifenol yang umumnya terdapat pada rimpang kunyit (*Curcuma longa* L.). Setelah pemberian peroral, kurkumin dalam tubuh akan segera dimetabolisme melalui proses reduksi maupun konjugasi. Oleh karena itu, kadar kurkumin di dalam darah sangat kecil sehingga diperlukan metode bioanalisis yang selektif dan sensitif. Metode Kromatografi Cair Kinerja Ultra Tinggi ? Tandem Spektrometer Massa (KCKUT-SM/SM) yang spesifik dan cepat telah dikembangkan dan divalidasi untuk menetapkan kadar kurkumin dalam plasma manusia menggunakan diazepam sebagai baku dalam. Pemisahan dilakukan menggunakan kolom C18 Acquity® Waters, UPLC BEH 1,7 μm, 2,1 x 100 mm, fase gerak asam format 0,15% - Asetonitril (50:50), laju alir 0,5 mL/menit dengan metode preparasi sampel ekstraksi cair-cair menggunakan campuran larutan etil asetatmetanol (95:5). Mode ionisasi yang digunakan adalah multiple reaction monitoring (MRM) dengan mode Electrospray ionization positif dengan nilai m/z berturut-turut 369,05 > 176,95 dan m/z 284,95 > 193 untuk kurkumin dan diazepam. Metode bioanalisis menunjukkan presisi dan akurasi yang baik dengan nilai % KV dan % bias < 15% untuk semua konsentrasi (QCL, QCM dan QCH) dengan nilai kurva kalibrasi yang linear (r = 0,999) pada rentang 1 ? 100 ng/mL dan nilai LLOQ untuk senyawa kurkumin sebesar 1,0 ng/mL. Metode ini telah diaplikasikan untuk menentukan kadar kurkumin dalam plasma 1 orang sehat yang telah diberi sediaan kurkumin 1800 mg. Dari penelitian diperoleh hasil tidak ditemukannya kurkumin dalam bentuk bebas, tetapi bentuk kurkumin terglukuronidasi dan tersulfatasi. Perbandingan antara jumlah terglukuronidasi dan tersulfatasi 4:1. Metode analisis yang diperoleh sudah memenuhi kriteria validitas menurut Guidance EMEA 2011 dengan sensitivitas yang tinggi sehingga dapat diaplikasikan untuk studi in-vivo

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ABSTRACT

Curcumin is a polyphenol, found in the spice turmeric from the rhizome of the herb *Curcuma Longa*. After oral administration, Curcumin undergoes rapid metabolism by conjugation and reduction. Curcumin levels are generally low so that the required bioanalytical method is selective and sensitive. A simple, specific and rapid UPLCMS/

MS method has been developed and validated for the estimation of curcumin in human plasma, using diazepam as internal standard (IS). The separation using UPLC BEH C18 column 1.7 μ m, 2,1 x 100 mm Acquity® Waters; 0.15% formic acid - acetonitril (50:50, v/v) as mobile phase; flow rate 0.5 mL/min; using liquid-liquid extraction with the mixture of ethyl acetate-methanol (95:5) for the sample preparation. The ionization mode using electrospray ionization (ESI) detection in multiple reaction monitoring (MRM) in positive ionization mode. The MS/MS ion transitions monitored were m/z 369.05 >176.95 and 284.95 > 193 for curcumin and diazepam respectively. The method was proved to be precise and accurate (expressed as coefficient of variation, % CV and differentiation, % diif) was < 15% for all concentration (QCL, QCM and QCH) with a coefficient correlation (r = 0.999) and linearity range of 1 – 100 ng/mL, LLOQ for curcumin was 1 ng/mL. The Method was applicated to determine the level of curcumin in healthy subject after oral administration 1800 mg of curcumin dosage form. No Free curcumin was detected in plasma sample, but curcumin glucuronides and sulfates were detected in plasma subject. The ratio of glucuronide to sulfate was 4: 1. The analytical method fullfilthe criteria of validity by the EMEA Guidance 2011 with high sensitivity and it would be applicable to in-vivo study., Curcumin is a polyphenol, found in the spice turmeric from the rhizome of the herb

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