Analisis simultan 6-merkaptopurin, 6-metilmerkaptopurin, dan 6-tioguanosin-5-monofosfat dalam biosampling dried blood spot menggunakan kromatografi cair-tandem spektrometri massa = Simultaneous analysis of 6-mercaptopurine, 6-methylmercaptopurine, and 6-thioguanosine-5-monophosphate in dried blood spot using ultra performance liquid chromatography tandem mass spectrometry

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Abstrak

ABSTRAK
6-Merkaptopurin merupakan agen kemoterapi yang termasuk golongan antimetabolit analog purin. Penelitian ini bertujuan untuk menganalisis secara simultan 6-merkaptopurin 6-MP ,6-metilmerkaptopurin 6-MMP , dan 6-tioguanosin-5 39;-monofosfat 6-TGMP pada sampel darah kering dengan menggunakan kromatografi cair kinerja ultra tinggi-tandem spektrometri massa KCKUT-SM/SM . Sebanyak 60 ? ? L darah utuh ditotolkan pada kertas DBS-CAMAG, ditambahkan baku dalam 5-fluorourasil 5-FU kemudian diekstraksi menggunakan metanol 90 v/v . Analisis dilakukan dengan kolom Waters Acquity UPLC BEH AMIDA 1,7 ? ? m 2,1 x 100 mm dengan fase gerak campuran 0,2 v/v asam format dalam air minus;0,1 v/v asam format dalam asetonitril-metanol, elusi secara gradien dan laju alir 0,2 mL/menit. Deteksi massa dilakukan menggunakan Waters Xevo TQD dengan ionisasi electrospray ESI positif untuk 6-MP, 6-MMP, 6-TGMP dan ESI negatif untuk 5-FU dengan mode multiple reaction monitoring. Deteksi 6-MP, 6-MMP, 6-TGMP, 5-FU masing-masing adalah m/z 153,09 > 119,09; 167,17 > 126,03; 380,16 > 168,00 ; 129,09 > 42,05. Metode ini linier dengan kisaran 25,5 ndash;1020 ng/mL untuk 6 MP, 6-MMP, dan 6-TGMP. Metode ini valid untuk analisis 6-MP, 6-MMP, dan 6-TGMP pada sampel darah kering secara simultan secara in vitro sesuai dengan pedoman European Medicines Agency
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ABSTRACT
6-Mercaptopurine is a chemotherapeutic agent of the antimetabolite class. This study aims to analyze simultaneous validation of 6-mercaptopurine 6-MP , 6-methylmercaptopurine 6-MMP , and 6-thioguanosine-5 rsquo;-monophosphate 6-TGMP in dried blood spot DBS using ultra performance liquid chromatography-tandem mass spectrometry UPLC-MS/MS . An accurate volume of 60 ? ? ? ? ? ? ? ? L blood was spotted onto DBS-CAMAG paper and then extracted using methanol 90 v/v containing an internal standard of 5-fluorouracil 5-FU . Separation was performed using a Waters Acquity UPLC BEH AMIDA column 1.7 ? ? ? ? ? ? ? ? m 2.1 x 100 mm with a mobile phase mixture of 0.2 v/v formic acid in water minus;0.1 v/v formic acid in acetonitrile-methanol with gradient elution and flow rate of 0.2 mL/min. Mass detection was done using Waters Xevo TQD with positive electrospray ionization ESI for 6-MP, 6-MMP, 6-TGMP and negative ESI for 5-FU, in multiple reaction monitoring mode. Detection rates of 6-MP, 6-MMP, 6-TGMP and 5-FU were m/z 153.09 > 119.09; 167.17 > 126.03; 380.16 > 168.00 ; 129.09 > 42.05, respectively. This method is linear across the range 25.5 ndash;1020 ng/mL for 6-MP, 6-MMP and 6-TGMP. This method is valid for the in vitro simultaneous analysis of 6-MP, 6-MMP and 6-TGMP in DBS, based on European Medicine Agency guidelines.