Studi farmakokinetika favipiravir dalam volumetric absorptive microsampling menggunakan kromatografi cair kinerja ultra tinggi-tandem spektrometri massa = Pharmakokinetic study of favipiravir in volumetric absorptive microsampling using ultra performance liquid chromatography-tandem mass spectrometry

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Abstrak

Favipiravir adalah agen antivirus yang selektif dan dapat digunakan untuk menghambat enzim RNA-dependent RNA polimerase (RdRp) dari virus RNA yang digunakan dalam terapi COVID-19. Favipiravir sebagai obat COVID-19 masih terus diteliti, terutama mengenai efek terapi yang ditimbulkan dari favipiravir. Pada penelitian ini dilakukan melalui studi farmakokinetik dalam sampel Volumetric Absorptive Microsampling (VAMS) yang cocok digunakan pada masa pandemi untuk menghambat penyebaran virus. Sampel yang digunakan dalam penelitian ini merupakan darah yang diambil dari enam subjek sehat yang telah diberikan tablet oral favipiravir Avigan® 200 mg pada jam ke-0 (pre-dose); 0,083; 0,167; 0,33; 0,5; 0,75; 1; 1,5; 2; 4; 6; 8; dan 12 jam setelah pemberian obat. Kondisi kromatografi yang digunakan adalah kolom Acquity UPLC BEH C18 (2,1 x 100 mm; 1,7 um); fase gerak asam format 0,2% dalam air – asetonitril (50:50 %v/v); dan asiklovir sebagai baku dalam. Profil farmakokinetika favipiravir dalam sampel VAMS memberikan hasil rata-rata AUC0-12h sebesar 8016,98 0-8075,45 ng.jam/mL; konsentrasi maksimum (Cmaks) dari keenam subjek sehat berkisar antara 3684,06 – 5338,38 ng/mL dengan rata-rata konsentrasi maksimum sebesar4501,02 ± 680,63ng/mL; waktu puncak (tmaks) keenam subjek adalah 0,5 jam; dan rata-rata waktu paruh (t1/2) 1,51 ± 0,15

.....Favipiravir is a selective antivirus agent that is capable to hinder the presence of RNA- dependent RNA polymerase (RdRp) enzyme from the RNA-virus used in COVID-19 therapy. The study of favipiravir as a COVID-19 drugs still being carried out regarding the therapeutic effects caused by favipiravir. During the pandemic, the microsampling such as Volumetric Absorptive Microsampling become the alternative for collecting the blood because it can inhibit the virus transferred. Therefore, in this study, six healthy subjects were tested for favipiravir content with the use of Volumetric Absorptive Micro- sampling (VAMS) that is safe for use. Blood samples were taken before the dose, and at t+0.083; 0.167; 0.33; 0.5; 0.75; 1; 1.5; 2; 4; 6; 8; and 12 hours after the dose of favipiravir Avigan® 200mg. By using Ultra-Performance Liquid Chromatography – Tandem Mass Spectometry (UPLC-MS/MS), pharmacokinetic study was done in order to obtain parameters such as AUC0-12h AUC0-, Cmax, Tmax, and t1/2. The chromatographic conditions used in the experiment were Acquity UPLC BEH C18 (2.1 x 100 mm; 1.7 um) column; mobile phase of formic acid 0.2% in water – acetonitrile (50:50 %v/v); injection volume of 10 l; flow rate of 0.15 mL/min; column temperature of 50°C; acyclovir as internal standard; and analysis time was 3.5 minutes. Pharmacokinetic profile of favipiravir content in the VAMS sample generates AUC0-12h was 8016.98 ± 1135.89 ng.hour/mL; AUC0- was 8075.45 ± 1139.97 ng.hour/mL; a maximum concentration (Cmax) ranging from 3684.06 to 5338,38 ng/mL, averaging at 4501.02 ± 680.63 ng/mL; peak time (tmax) of the six subjects was at 0.5 hour; and half-time (t1/2) was 1.51 ± 0.15 hours.