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Improving the Dissolution Rate and the Bioavailability of Favipiravir by Solid Dispersion with Curcumin

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SUMMARY. **Favipiravir is an anti-viral agent that inhibits RNA-dependent RNA polymerase of several RNA viruses and is approved for the treatment of influenza in Japan. It has a role as an antiviral drug, an anti-coronaviral (COVID-19) agent but the poor solubility of the favipiravir in the aqueous media of the human body cause a reduction in the effectiveness and bioavailability. In the current work, the favipiravir was formulated for the first time as solid dispersed system with curcumin to improve dissolution property and antiviral activity during treatment of Covid-19. Binary and ternary mix of favipiravir and curcumin with/without soluplus were prepared and characterized by Differential Scanning Calorimetry (DSC), Powder X-ray Diffractometry (PXRD) and Fourier Transform Infrared Spectroscopy (FTIR) and subjected to the dissolution test by apparatus I according to the European Pharmacopeia. The antiviral activity was measured by its cytotoxicity against A549-hACE2 cells. The results revealed that there was a reduction in the crystallinity of both binary and ternary mixtures with an enhancement of the dissolution in comparison with the pure drug which accompanied by an improvement in the antiviral activity which is promising results that need further .**

RESUMEN. Favipiravir es un agente antiviral que inhibe la ARN polimerasa dependiente de ARN de varios virus ARN y está aprobado para el tratamiento de la influenza en Japón. Tiene un papel como medicamento antiviral, un agente anti-coronaviral (COVID-19) pero la poca solubilidad del favipiravir en los medios acuosos del cuerpo humano causa una reducción en la efectividad y biodisponibilidad. En el trabajo actual, favipiravir se formuló por primera vez como un sistema disperso sólido con curcumina para mejorar la propiedad de disolución y la actividad antiviral durante el tratamiento de Covid-19. Se prepararon mezclas binarias y ternarias de favipiravir y curcumina con/sin soluplus y se caracterizaron por calorimetría diferencial de barrido (DSC), difractometría de rayos X en polvo (PXRD) y espectroscopia infrarroja transformada de Fourier (FTIR) y se sometieron a la prueba de disolución por el aparato I de acuerdo con a la farmacopea europea. La actividad antiviral se midió por su citotoxicidad contra las células A549-hACE2. Los resultados revelaron que hubo una reducción en la cristalinidad de las mezclas binarias y ternarias con una mejora de la disolución en comparación con el fármaco puro que se acompañó de una mejora en la actividad antiviral, resultados prometedores que necesitan más estudio.

KEY WORDS: antiviral activity. Covid-19, curcumin, favipiravir, pterostilbene, solid dispersion.

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