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Formulation Development and Optimization of Flurbiprufen and Ranitidine Bilayer Tablet Designed by Central Composite Rotatable Design (CCRD) and Their *In Vitro* Kinetic Studies

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***SUMMARY*. Bilayer tablets of flurbiprofen SR and ranitidine IR was developed by using HPMC K4-M and colloidal silicon dioxide. Twenty formulations were planned by using design expert and micromeritic properties were analyzed for selection of six suitable formulations. Single punch machine was used for compression of bilayer tablets and physicochemical and quality control evaluation was performed successfully. Weight variation, hardness, friability and disintegration time were evaluated by pharmacopeial procedures. Release of ranitidine IR was studied for 60 min, while flurbiprofen SR was analysed for 24 h. *In vitro* kinetic studies like zero order, first order, Hixson-Crowell, and Weibull were applied to ranitidine IR formulation and flurbiprofen SR formulation was evaluated by zero order, first order, Higuchi, Korsmeyer-Peppas, Hixson-Crowell and Weibull. Regression values of a first order in IR and zero order in SR were found to more than 0.97 and Weibull model was used to explain the shape factor formulation. S1 formulation was considered as the best one and was selected for further *in vivo* studies.**

RESUMEN. Se desarrollaron comprimidos bicapa de flurbiprofeno SR y ranitidina IR mediante el uso de HPMC K4-M y dióxido de silicio coloidal. Veinte formulaciones fueron planeadas usando diseño experto y se analizaron las propiedades micromeríticas para la selección de seis formulaciones. Se utilizó una compresora simple para la obtención de los comprimidos bicapa y la evaluación de las propiedades físico-químicas y de control de calidad fueron exitosas. La variación de peso, dureza, friabilidad y tiempo de desintegración fueron evaluados por procedimietnos farmacopeicos. La liberación de ranitidina IR se estudió durante 60 min y flurbiprofeno SR durante 24 h. Estudios cinéticos *in vitro* de orden cero, primer orden, Hixson-Crowell y Weibull fueron aplicados a la formulación de ranitidina IR., en tanto que la formulación de flurbiprofeno SR fue evaluada mediante estudios de orden cero, primer orden, Higuchi, Korsmeyer-Peppas, Hixson-Crowell y Weibull. Los valores de la regresión de primer orden en IR y de orden cero en SR resultaron superiores a 0.97 y el modelo de Weibull se usó para explicar la formulación del factor de forma. La formulación S1 se consideró la mejor y fue seleccionada para posteriores estudios *in vivo*.

KEY WORDS: Hydroxypropylmethylcellulose, Immediate release, *In vitro* kineticand slow release.

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