BIOAVAILABILITY AND BIOEQUIVALENCE STUDIES OF CARBAMAZEPINE FORMULATIONS IN CUBAN POPULATION.

Ph,D. Alejandro Saúl Padrón Yaquis *Lic. Lisette Martínez Miranda, *Lic. Narda María Jiménez Alemán, *Lic. Jorge Ernesto Calero Carbonell, **Dr. Carlos A. González Delgado (M.Sc.), **Dra. Alina Díaz Machado **Lic. Armando Correa Fernández, **Lic. Lourdes Olivera Lluano.
Centre for Pharmaceuticals Research and Development. BioCubaFarma. Cuba

TNTRODUCTION

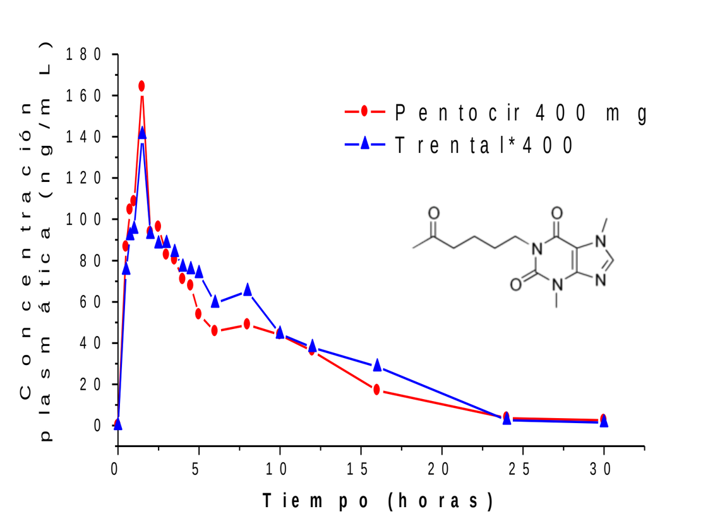
The Cuban industry produces about of 70 % of pharmaceuticals (generic) included in the National List of Basic Drugs. The focus of this work is to share with pharmaceutical scientists, academic researchers, regulators and key opinion leaders,the Cuban experiences on bioavailability and Bioequivalence Studies of Pharmaceuticals.

Through a selected example (carbamazepine) we disclose the several stages of the studies, according to national and international regulations.

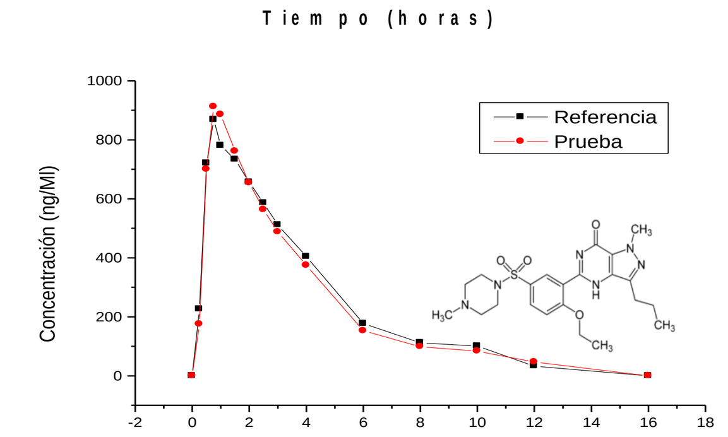
The focus of this work is to share with pharmaceutical scientists, academic researchers, regulators and key opinion leaders, the Cuban experiences on bioavailability and Bioequivalence Studies of Pharmaceuticals.

Through selected example we disclose the several stages, such as analytical method selection, information required for the protocol concerning analytical method development and validation, as well as design, conduction and statistical analysis of the studies, according to national and international regulations

SOME BIOEQUIVALENCE STUDIES CARRIED OUT LATELY



Parámetros farmacocinéticos	Pentocir 400 mg	Trental*400 (Hoechst-Marion, Roussel)
$C_{máx}$ (ng/mL)	164.10	141.10
$T_{máx}$ (h)	1.80	2.70
$t_{½}$ (h)	4.71	4.60
AUC (ng/h/mL)	963.70	980.10



MP	IC		Límites		Concl
	WL_90 _Lower	WL_90_ Upper	Lower	Upper	
Ln(Cmáx)	93.48	106.52	80.00	125.0	BE
Ln(AUClast)	90.83	109.17	80.00	125.0	BE

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Artículos originales

AWARD BY ACADEMY OF SCIENCE OF CUBA

Pedro Kourí Institute

Bioequivalence study: generic and trade formulations of stavudine, lamivudine, zidovudine and indinavir in Cuban HIV-infected subjects

Alicia Tarinas Reyes,1 Rolando D. Tápanes Peraza,2 Lizette Gil del Valle,3 Daniel González Rubio,4 Osvaldo Peraza,4 Alejandro Saúl Padrón,2 Alina Martínez Rodríguez,5 Mylai Orta Gutiérrez,6 Geisy Ferrer Linares7 y Pérez Ávila8

SELECTED EXAMPLE

Carbamazepine was discovered in 1953. It was first marketed in 1962.[7] It is available as a generic medication. It is on the WHO Model List of Essential Medicines, the most important medications needed in a basic health system.

The time-courses of plasma carbamazepine concentrations were followed in apparently healthy adult subjects who, at different times, took single oral drug dose of 200 mg. Volunteers received a single dose with 240 mL of water on each treatment days separated by a 2 week washout period. After dosing, serial blood samples were collected for a period of 190 h. plasma was analyzed for carbamazepine by a sensitive, reproducible and accurate HPLC method. Various pharmacokinetic parameters were calculated from plasma concentration of four (two Cuban, two imported) formulations. Correlation of dissolution test and pharmacokinetic parameters were discussed, as well as variability intra formulation, intra voluntaries and the sex influences on these parameters.

Based on statistical inferences, it was concluded that carbamazepine formulations have similar tends in Cuban population. source. S

Alejandro Saúl Padrón Yaquis
E-mail:
alejandro.padron@infomed.sld.cu<
alejandro.padron@cidem.cu
Telephone: (537) 781-19-44, 7881-00-09
Post: General Director

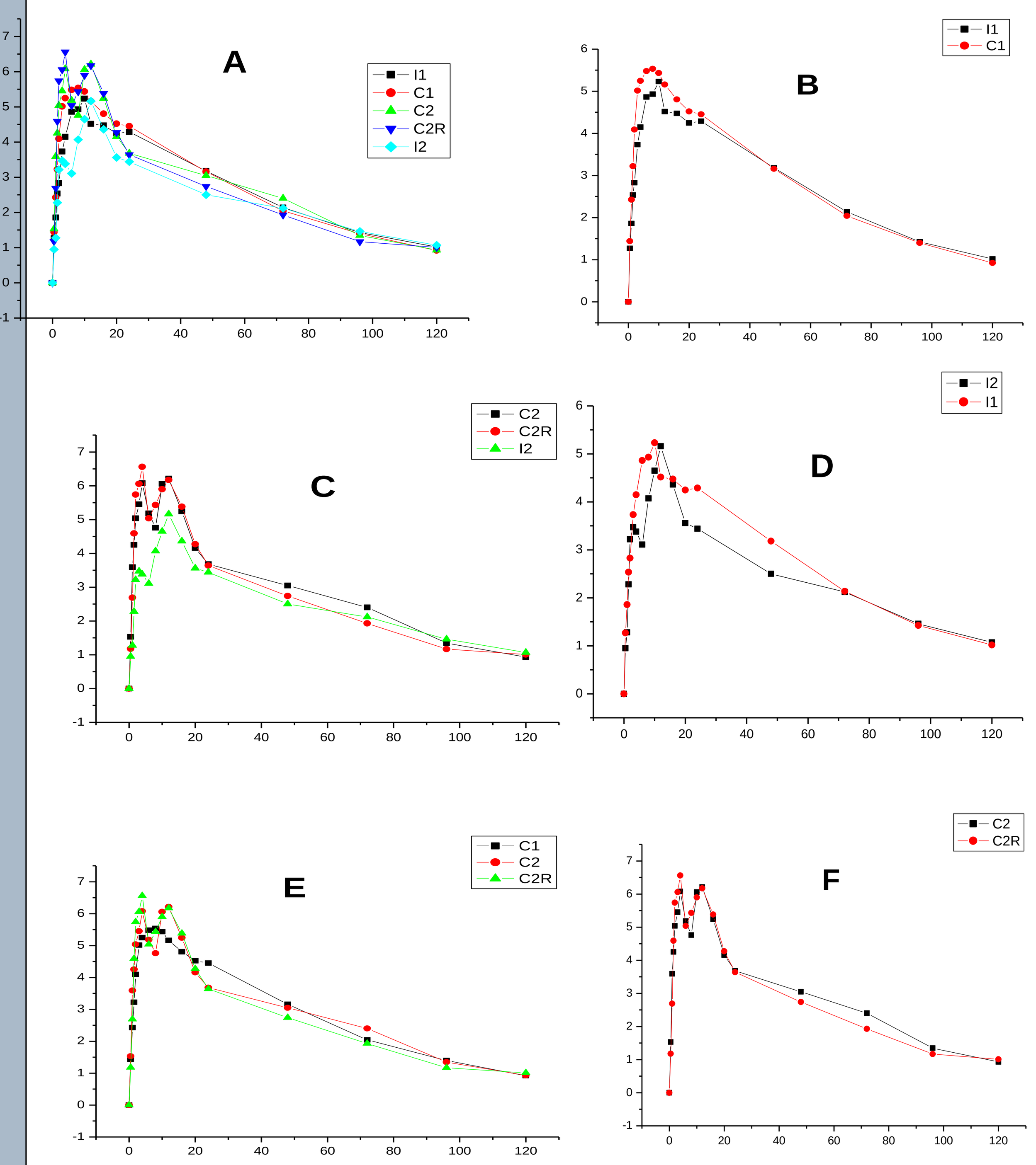
DISOLUTION TEST

FORMULATION	TEST I	TEST II	TEST III
IMPORTED I_1	(60 min) 98.4 ± 2.4 **Conform**	(15 min) 64.2 ± 6.9 (60 min) 98.4 ± 2.4 **Conform**	(15 min) 64.2 ± 6.9 (60 min) 98.4 ± 2.4 **Conform**
IMPORTED I_2	(60 min) 99.8 ± 2.3 **Conform**	(15 min) 68.5 ± 3.4 (60 min) 99.8 ± 2.3 **Conform**	(15 min) 68.5 ± 3.4 (60 min) 99.8 ± 2.3 **Conform**
CUBAN C_1	(60 min) 99.8 ± 2.3 **Conform**	((15 min) 61.2 ± 6.3 (60 min) 94.6 ± 4.1 Conform	(15 min) 61.2 ± 6.3 (60 min) 94.6 ± 4.1 Conform
CUBAN C_2	(60 min) 95.7 ± 5.5 **Conform**	(15 min) 93.9 ± 3.9 (60 min) 95.7 ± 5.5 **does not comply**	(15 min) 93.9 ± 3.9 (60 min) 95.7 ± 5.5 **does not comply**
CUBAN C_{2R}	(60 min) 94.4 ± 4.7 **Conform**	(15 min) 92.6 ± 5.5 (60 min) 94.4 ± 4.7 **does not comply**	((15 min) 92.6 ± 5.5 (60 min) 94.4 ± 4.7 **does not comply**

RESULTS

	T_{max}	C_{max}	AUC_t	Ke	$t_{1/2}$	Vz/F	Cl/F	MRT_t	MRT_I
IMPORTED I_1 (n=25)									
Media	8.560	5.929	324.6	0.017	45.31	32.54	0.521	45.26	70.87
CV (%)	22.9	16.4	13.4	40.4	30.9	22.1	20.0	9.1	26.3
IMPORTED I_2 (n=12)									
Media	9.125	6.418	285.7	0.017	53.56	38.64	0.565	45.39	82.44
CV (%)	67.6	24.0	16.1	54.7	56.5	33.9	28.5	14.0	46.2
CUBAN C_1 (n+25)									
Media	7.120	5.789	328.3	0.018	43.48	42.79	0.655	42.56	66.17
CV (%)	39.4	23.6	23.6	34.6	31.1	151.7	114.6	9.4	26.6
CUBAN C_2 (n=12)									
Media	9.000	7.387	320.4	0.021	38.66	28.22	0.547	41.65	62.98
CV (%)	46.7	12.9	17.4	40.2	47.1	26.9	22.7	16.5	37.7
CUBAN C_{2R} (n=12)									
Media	6.375	7.630	302.8	0.020	45.35	32.62	0.568	39.69	66.35
CV (%)	69.8	24.2	13.0	48.5	58.6	31.1	25.7	14.4	45.4

RESULTS



REULTS

	T_{max}	C_{max}	AUC_l	Ke	$t_{1/2}$	Vz/F	Cl/F
I_1 FEMALE (n=7)							
Media	8.000	5.846	335.600	0.018	46.760	30.943	0.504
CV (%)	32.3	8.2	13.9	59.5	41.0	22.2	27.8
I_1 MALE (n=18)							
Media	8.778	5.962	324.363	0.016	47.403	34.136	0.517
CV (%)	19.4	18.8	13.2	31.4	31.3	22.0	17.4
I_2 FEMALE (n=4)							
Media	7.500	6.173	286.245	0.016	54.584	41.621	0.581
CV (%)	55.0	34.5	23.1	55.9	52.5	38.0	29.0
I_2 MALE (n=8)							
Media	9.938	6.540	293.909	0.014	66.038	42.712	0.519
CV (%)	71.4	20.0	12.5	52.4	63.6	37.6	31.3
FEMALE C_1 (n=7)							
Media	6.286	5.970	334.555	0.018	43.424	29.674	0.508
CV (%)	52.5	9.8	14.9	33.9	32.6	12.0	25.8
MALE C_1 (n=18)							
Media	7.444	5.718	330.834	0.017	44.705	47.909	0.703
CV (%)	35.2	27.7	26.4	30.5	28.5	154.9	125.2
FEMALE C_2 (n=4)							
Media	12.000	7.383	333.564	0.022	34.515	28.140	0.548
CV (%)	27.2	15.9	26.3	34.0	27.1	41.3	20.5
MALE C_2 (n=8)							
Media	7.500	7.389	329.288	0.017	50.648	32.564	0.491
CV (%)	52.4	12.4	10.1	45.6	54.3	33.0	21.4
C_{2R} FEMALE (n=4)							
Media	9.500	8.158	304.048	0.024	32.281	26.287	0.588
CV (%)	52.6	26.8	9.9	35.2	34.3	23.5	19.6
C_{2R} MALE (n=8)							
Media	4.813	7.366	312.846	0.017	64.299	38.660	0.527
CV (%)	72.0	23.8	15.1	64.2	88.7	41.3	32.2

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OTHERS STUDIES CARRIED OUT

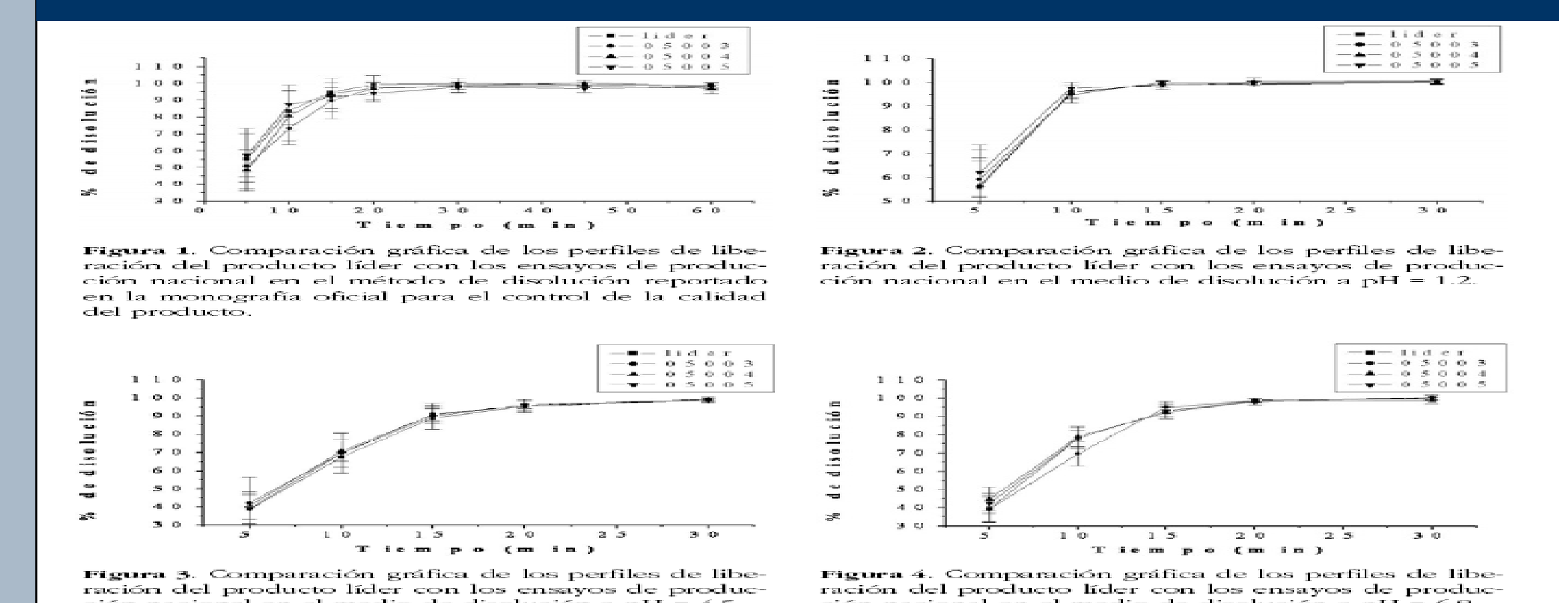

Figura 1. Comparación gráfica de los perfiles de liberación del producto líder con los ensayos de producción nacional en el método de disolución reportado en la monografía oficial para el control de la calidad del producto.

Figura 2. Comparación gráfica de los perfiles de liberación del producto líder con los ensayos de producción nacional en el medio de disolución a pH = 1.2.

Figura 3. Comparación gráfica de los perfiles de liberación del producto líder con los ensayos de producción nacional en el medio de disolución a pH = 4.5.

Figura 4. Comparación gráfica de los perfiles de liberación del producto líder con los ensayos de producción nacional en el medio de disolución a pH = 6.8.

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Original Article
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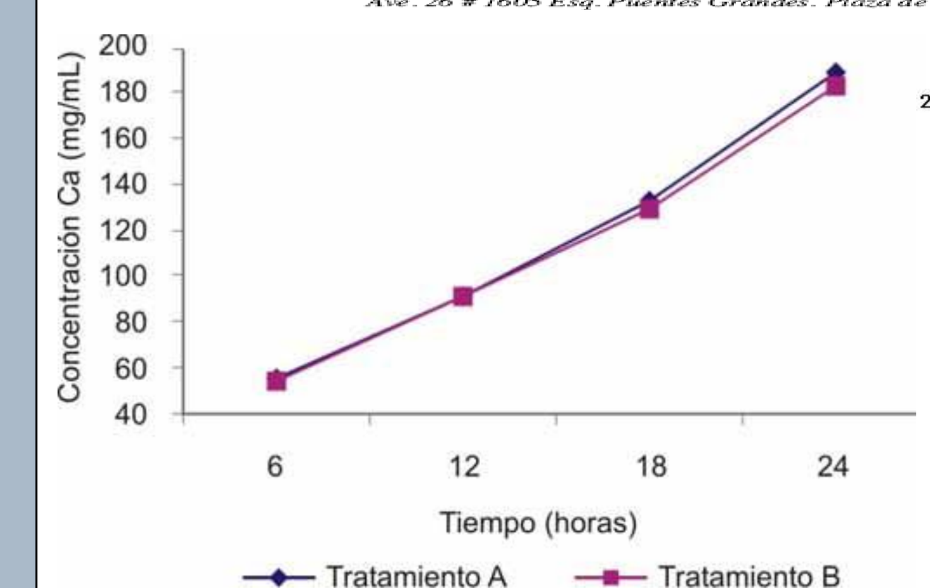
Evaluación Comparativa de la Liberación *in vitro* de una Formulación de Ribavirina 200 mg Producida en Cuba contra Rebetol®, Producto Innovador

Narda M. JIMÉNEZ ALEMÁN*, Alejandro S. PADRÓN YAQUIS & Jorge E. Calero CARBONEL
Departamento de Bioequivalencia. Centro de Investigación y Desarrollo de Medicamentos (CIDEM). Ave. 26 # 1605 Esq. Puentes Grandes. Plaza de La Revolución. C. Habana. Cuba.



2. Resultados de las mediciones de calcio en cada tratamiento (mg/L)

Tiempo	Tratamiento A	Tratamiento B	p*
	Media ± DE	Media ± DE	
Basal	172,64 ± 80,11	161,21 ± 81,07	0,1576
24	188,47 ± 74,40	181,95 ± 86,33	0,1557
De 0 a 6	55,79 ± 26,94	54,46 ± 28,32	0,2040
De 6 a 12	34,65 ± 21,66	36,33 ± 13,33	0,2366
De 12 a 18	42,50 ± 26,08	37,96 ± 22,93	0,0055
De 18 a 24	55,53 ± 28,93	53,21 ± 26,27	0,0725

Tratamiento A: CalcidolÒ; tratamiento B: Carbonato de calcio.

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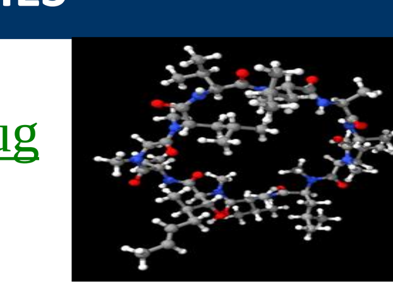
Centro de Investigaciones y Desarrollo de Medicamentos

Estudio de biodisponibilidad comparada del Calcidol Ò tabletas, a dosis única en voluntarios sanos

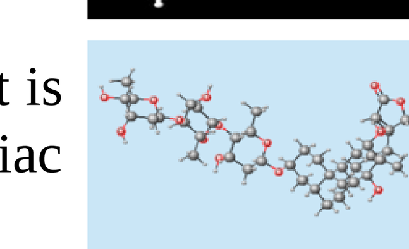
Jorge E. Rodríguez Chanfrau,1 Humberto Guanche Garcell,2 Grisel Soto Argüelles,3 Alberto Hernández Rodríguez,4 Marta Palencia García5 y Zenia Pardo Ruíz6

CURRENT BIOEQUIVALENCE STUDIES

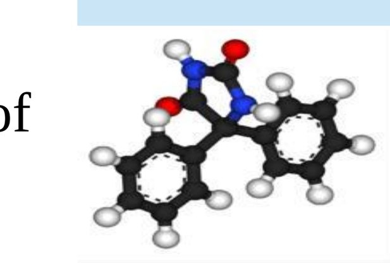
Cyclosporin A, is an immunosuppressant drug widely used in post-allogeneic organ transplant



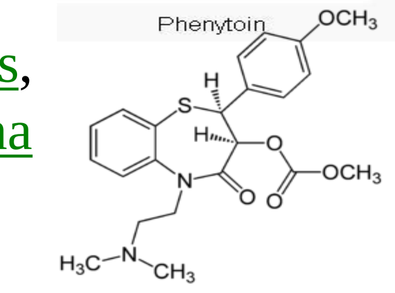
Phenytoin is a commonly used antiepileptic. it is an option in the treatment of certain cardiac arrhythmias.



Digoxin, is widely used in the treatment of various heart conditions,



Diltiazem a class of calcium channel blockers, used in the treatment of hypertension, angina pectoris, and some types of arrhythmia.



Contact information

Alejandro Saúl Padrón Yaquis
E-mail:
alejandro.padron@infomed.sld.cu<
alejandro.padron@cidem.cu
Telephone: (537) 781-19-44,
Post: General Director

Academic background. * - Validated by the Cuban Ministry of Higher Education.
***Engineer,** Subject of Specialization: Chemical and nuclear Technologies. Russian Chemical University D. I. Mendeleiev. Location: Moscow.
***Master of Science in chemistry (M.Sc),** Subject of Specialization: Physical Chemistry. Russian Chemical University D. I. Mendeleiev. Location: Moscow. Year awarded: 1992.
Doctor in Pharmaceutical Sciences (PhD), Subject of Specialization: Technology and Control of Drugs. Year awarded: 2002.