

Berberine Hydrochloride 의 吸着에 關한 研究

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Study on the Adsorption of Berberine Hydrochloride.

When a large quantity of insoluble drugs was added into a solution containing a small amount of soluble drugs, the latter was adsorbed to the former. Their adsorption was expected to alter the drug activity. Berberine hydrochloride (BH) was selected as a soluble drug and tested with frequently combined insoluble drugs and antacids for their adsorption phenomena in purified water, gastric and intestinal fluid test solutions, respectively. The adsorption isotherms of kaolin and natural aluminum silicate with BH in the three media fitted the Langmuir (LM) equation, and that of talc in purified water and gastric fluid fitted it, but in intestinal fluid it fitted the Freundlich equation. The adsorption isotherm of aluminum hydroxide fitted the LM equation only in intestinal fluid. The degree of adsorption of BH in purified water and gastric fluid is in the following order: magnesium trisilicate, kaolin, natural aluminum silicate and talc; in intestinal fluid: magnesium trisilicate, kaolin, talc, natural aluminum silicate and aluminum hydroxide. Magnesium stearate did not adsorb BH.

多量の 不溶性 藥品에 少量의 可溶性藥品이 配合될 경우 前者에 後者が 吸着되고 따라서 그 藥効에 變化를 일으키기 豫상되어 藥品 吸着에 對한 研究가 行하여지고 있다.

Ridout¹⁾는 atropine水溶液에서의 kaolin의 吸着에 對하여 또한 Kubo등은²⁾ atropine의 數種 不溶性 藥品과의 吸着에 對하여 또 最近에는 Nogami등은³⁻⁶⁾ 物理藥劑學的인 面에서 여러 藥品의 吸着에 對한 動力學的인 手法으로 研究하여 報告하고 있다.

著者들은 整腸殺菌劑로 많이 쓰이고 있는 可溶性 藥品인 berberine hydrochloride와 이와 配合 常用되고 있는 不溶性 藥品 및 制酸劑 數種을 選擇하여 精製水, 人工胃液, 人工腸液中에서의 그 吸着現象을 觀察하여 知見을 얻었기에 이를 報告하는 바이다.

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實驗方法

Berberine hydrochloride—서울약품에서 제공한 Berberine hydrochloride를 熱湯으로 數回 再結晶하여 使用하였다.

不溶性 藥品으로 Talc, Kaolin(Yamata Co.), 天然珪酸알미늄(Harmoto Co.), Aluminum hydroxide (Kishida Chemical Co.), Magnesium stearate (Iwaki Co.), Magnesium trisilicate (Iwaki Co.)를 粒子度의 크기를 一定하게 하기 위하여 200 mesh의 체를 통과한 것을 105°에서 4時間 乾燥하여 使用하였다.

Berberine hydrochloride의 定量—Berberine hydrochloride를 黃酸메시케이타에서 恒量으로 될 때까지 乾燥하여 再蒸留수에 溶解하여 波長 420m μ 에서 吸光度를 測定하여 따로 만든 檢量曲線에서 berberine hydrochloride의 量을 求하였다.

吸着平衡到達時間測定—Berberine hydrochloride溶液(50 μ g/ml) 50ml 및 不溶性 藥品各 00mg을 取하여 100ml의 삼각파라스크에 넣고 30°恒溫槽에서 15分마다 振盪하고 一定時間(1, 2, 3, 4, 5, 24時間)後 遠心分離 (13,000 rpm)하여 上澄液에 對하여 berberine hydrochloride의 量을 測定하였다.

이때 對照試驗을 하였다.

吸着試驗—不溶性 藥品 100mg을 正確히 秤取하여 100ml 삼각파라스크에 넣고 따로 berberine hydrochloride를 精製水, 人工胃液, 人工腸液에 溶解하여 ml 당 10, 20, 30, 40, 50 μ g를 含有하게 만든 液 50ml씩을 넣어 吸着平衡 到達時間 測定과 같은 操作으로 吸着量을 測定하였다.

實驗結果

吸着平衡到達時間測定—Berberine hydrochloride와 不溶性 藥品의 吸着平衡到達時間은 Table 1과 같다.

Table I—Time required for reaching equilibrium.

Insoluble drug	Time required for reaching equilibrium
Talc	1
Kaolin	2
Natural aluminum silicate	3
Aluminum hydroxide	2
Magnesium trisilicate	3

吸着試驗—吸着試驗의 結果를 Langmuir와 Freundlich의 吸着等溫式에 代入하면 Table 2-5와 같고 이것을 圖示하면 Fig. 1-8과 같다.

Table II—Adsorption of berberine hydrochloride on talc in purified water, simulated gastric fluid T.S. and simulated intestinal fluid T.S.

	Berberine HCl conc. $\mu\text{g/ml.}$	C $\mu\text{g/ml.}$	x $\mu\text{g/100mg}$	m=100mg $\frac{x}{m}$ ($\times 10^3$)	C/ $\left(\frac{x}{m}\right)$ ($\times 10^{-5}$)	log C	log x
Purified water	50	43.6	6.4	6.4	6.8125	1.6395	0.8062
	40	33.6	6.4	6.4	5.2500	1.5263	0.8062
	30	23.6	6.4	6.4	3.6871	1.3729	0.8062
	20	13.8	6.2	6.2	2.2258	1.1399	0.7924
	10	4.2	5.8	5.8	0.7241	0.6232	0.7634
Simulated gastric fluid T.S.	50	44.9	5.1	5.1	8.8039	1.6532	0.7076
	40	35.2	4.8	4.8	7.3333	1.5465	0.6812
	30	25.5	4.5	4.5	5.6666	1.4065	0.6532
	20	16.0	4.0	4.0	4.0000	1.2041	0.6021
	10	6.9	3.1	3.1	2.2258	0.8388	0.4914
Simulated intestinal fluid T.S.	50	39.8	10.2	10.2	3.9019	1.5999	1.0086
	40	30.5	9.5	9.5	3.2105	1.4843	0.9777
	30	21.3	8.7	8.7	2.4482	1.3284	0.9375
	20	12.5	7.5	7.5	1.6666	1.0969	0.8751
	10	4.2	5.8	5.8	0.7241	0.6128	0.7709

Table III—Adsorption of berberine hydrochloride on kaolin in purified water, simulated gastric fluid T.S. and simulated intestinal fluid T.S.

	Berberine HCl conc. $\mu\text{g/ml.}$	C $\mu\text{g/ml.}$	x $\mu\text{g/100mg}$	m=100mg $\frac{x}{m}$ ($\times 10^3$)	C/ $\left(\frac{x}{m}\right)$ ($\times 10^{-5}$)	log C	log x
Purified water	50	41.7	8.3	8.3	5.0240	1.6201	0.9191
	40	31.9	8.1	8.1	3.9382	1.5038	0.9085
	30	21.9	8.1	8.1	2.7037	1.3404	0.9085
	20	12.0	8.0	8.0	1.5000	1.0792	0.9031
	10	3.4	6.6	6.6	0.5151	0.5315	0.8195
Simulated gastric fluid T.S.	50	42.5	7.5	7.5	5.6566	1.6284	0.8751
	40	32.7	7.3	7.3	4.4794	1.5145	0.8633
	30	23.0	7.0	7.0	3.2857	1.3617	0.8451
	20	14.0	6.0	6.0	2.3333	1.1461	0.7782
	10	5.5	4.5	4.5	1.2222	0.7404	0.6532
Simulated intestinal fluid T.S.	50	39.3	10.7	10.7	3.6728	1.5944	1.0294
	40	29.7	10.3	10.3	2.8834	1.4728	1.0128
	30	21.0	9.0	9.0	2.3333	1.3222	0.9542
	20	12.6	7.3	7.3	1.7260	1.1004	0.8633
	10	5.5	4.5	4.5	1.2222	0.7404	0.6532

Table IV—Adsorption of berberine hydrochloride on natural aluminum silicate in purified water, simulated gastric fluid T.S. and simulated intestinal fluid T.S.

	Berberine HCl conc. μg/ml.	C μg/ml.	x μg/100mg	m=100mg x/m (×10 ⁵)	C / ($\frac{x}{m}$) (×10 ⁻⁵)	log C	log x
Purified water	50	42.2	7.8	7.8	5.4102	1.6253	0.8921
	40	32.2	7.8	7.8	4.1282	1.5079	0.8921
	30	22.5	7.5	7.5	3.0000	1.3522	0.8751
	20	12.8	7.2	7.2	1.7777	1.1072	0.8573
	10	3.9	6.1	6.1	0.6393	0.5911	0.7853
Simulated gastric fluid T.S.	50	45.2	4.8	4.8	9.4166	1.6551	0.6812
	40	35.3	4.7	4.7	7.5106	1.5478	0.6721
	30	25.5	4.5	4.5	5.6666	1.4065	0.6532
	20	15.8	4.2	4.2	3.7619	1.1987	0.6232
	10	6.5	3.5	3.5	1.8571	0.8129	0.5441
Simulated intestinal fluid T.S.	50	41.9	8.1	8.1	5.1728	1.6222	0.9085
	40	32.1	7.9	7.9	4.0633	1.5065	0.8976
	30	22.2	7.9	7.9	2.8461	1.3464	0.8921
	20	12.6	7.4	7.4	1.7027	1.1004	0.8692
	10	4.7	5.3	5.3	0.8868	0.6721	0.7243

Table V—Adsorption of berberine hydrochloride on aluminum hydroxide in simulated intestinal fluid T.S.

	Berberine HCl conc. μg/ml.	C μg/ml	x μg/100mg	m=100mg x/m (×10 ⁵)	C / ($\frac{x}{m}$) (×10 ⁻⁵)	log C	log x
Simulated intestinal fluid T.S.	50	42.6	7.4	7.4	5.7567	1.6294	0.8692
	40	32.9	7.1	7.1	4.6338	1.5172	0.8513
	30	22.9	7.1	7.1	3.2253	1.3598	0.8513
	20	12.9	7.1	7.1	1.8169	1.1106	0.8513
	10	4.2	5.8	5.8	0.7241	0.6232	0.7634

Langmuir equation

$$C / \left(\frac{x}{m} \right) = 1/ab + c/b$$

Freundlich equation

$$x = kC^{\frac{1}{n}}$$

$$\log x = \log k + \frac{1}{n} \log C$$

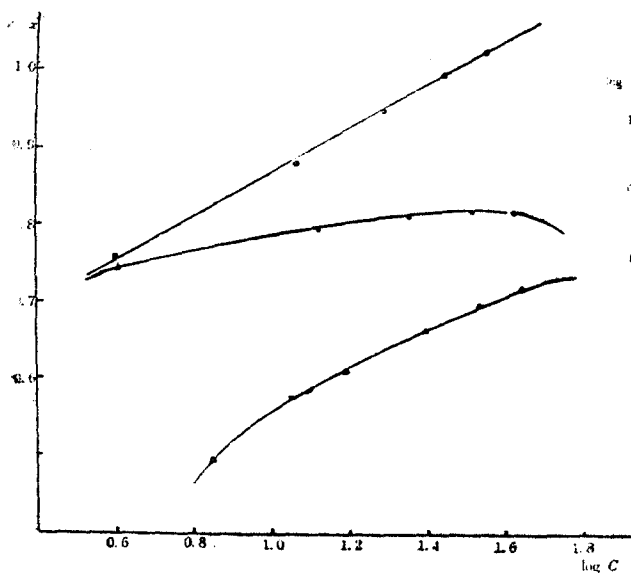


Fig. 1—Freundlich plots for adsorption of berberine hydrochloride on talc in purified water(●), simulated gastric fluid T.S.(△) and simulated intestinal fluid T.S.(○)

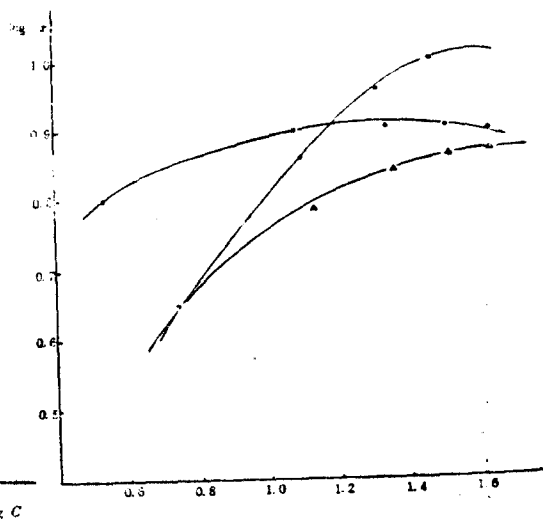


Fig. 2—Freundlich plots for adsorption of berberine hydrochloride on kaolin in purified water(●), simulated gastric fluid T.S.(△) and simulated intestinal fluid T.S.(○)

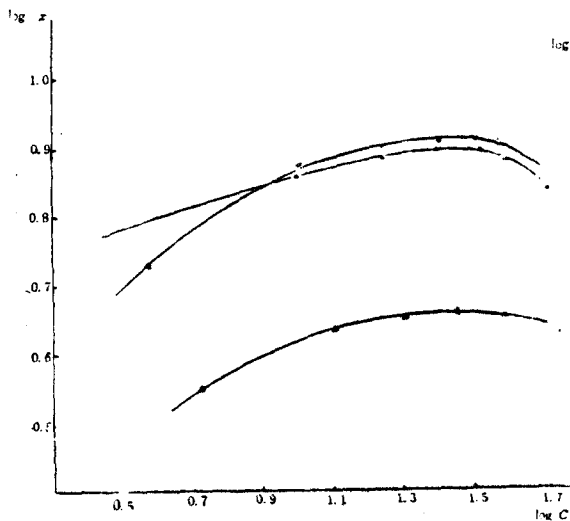


Fig. 3—Freundlich plots for adsorption of berberine hydrochloride on natural aluminum silicate in purified water(●), simulated gastric fluid T.S.(△) and simulated intestinal fluid T.S.(○)

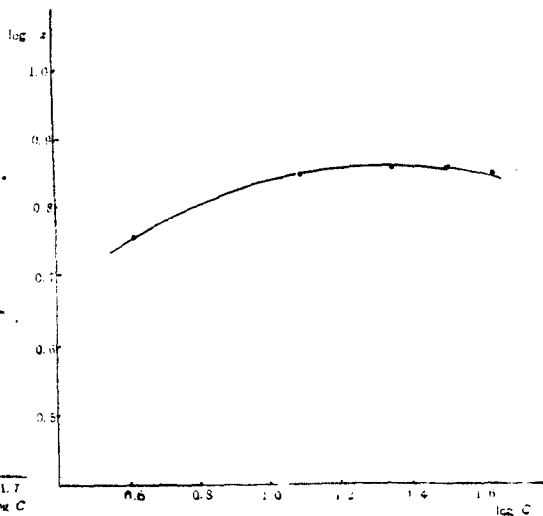


Fig. 4—Freundlich plots for adsorption of berberine hydrochloride on aluminum hydroxide in simulated intestinal fluid T.S.(○)

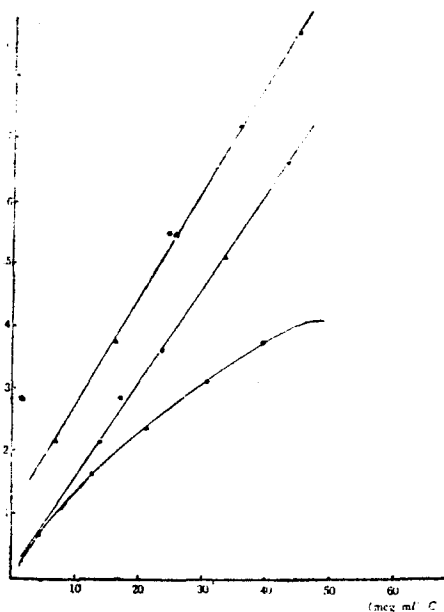


Fig. 5—Langmuir plots for adsorption of berberine on talc in purified water(●), simulated gastric fluid T.S.(▲) and simulated intestinal fluid T.S.(○)

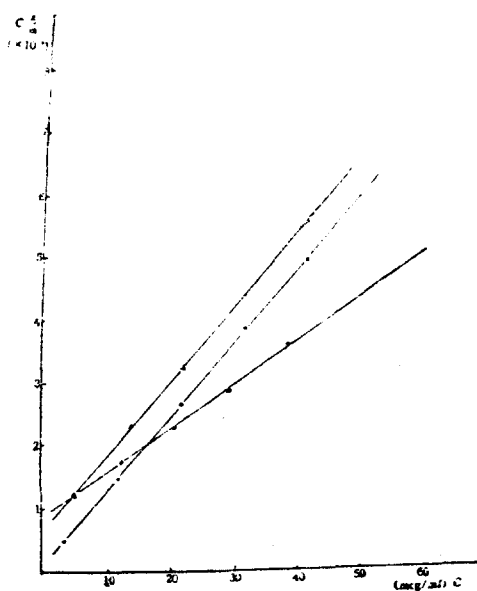


Fig. 6—Langmuir plots for adsorption of berberine hydrochloride on kaolin in purified water(●), simulated gastric fluid T.S.(▲) and simulated intestinal fluid T.S.(○)

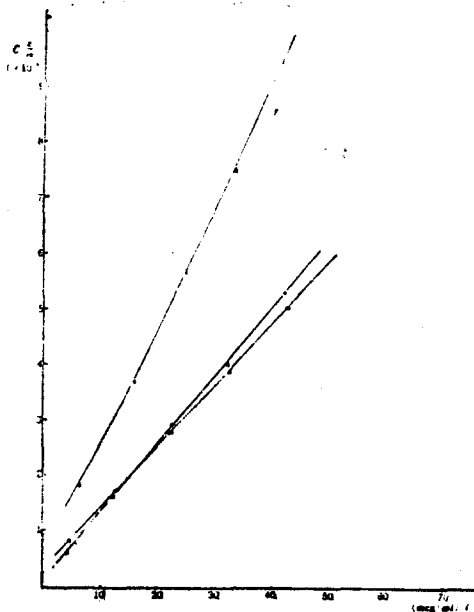


Fig. 7—Langmuir plots of adsorption of berberine hydrochloride on natural aluminum silicate in purified water(●), simulated gastric fluid T.S.(▲) and simulated intestinal fluid T.S.(○)

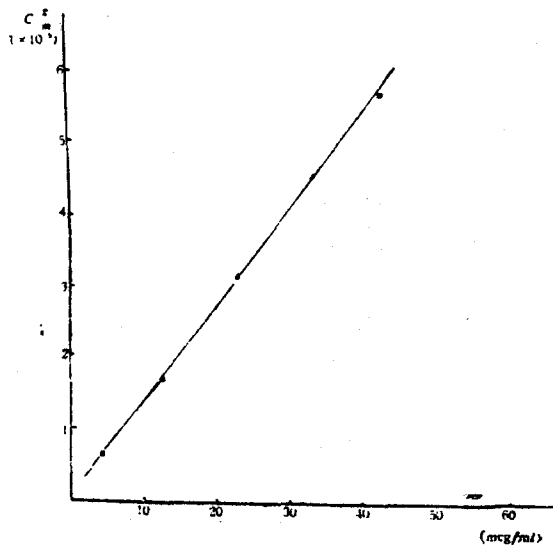


Fig. 8—Langmuir plots of adsorption of berberine hydrochloride on aluminum hydroxide in simulated intestinal fluids T.S.(○)

結 論

Berberine HCl와 不溶性 藥品과의 吸着現象을 볼 때 精製水, 人工胃液, 人工腸液中에서의 kaolin, 天然珪酸알미늄은 Langmuir의 吸着等溫式에 一致하고 精製水, 人工胃液中에서의 talc의 吸着은 Langmuir의 式에 一致되었으나 人工腸液에선 Freundlich의 吸着等溫式에 一致되었다. 또한 aluminum hydroxide는 人工腸液에서만 Langmuir의 式에 一致되었다.

吸着의 順에 있어서 精製水및 人工胃液中에서는 magnesium trisilicate, kaolin, 天然珪酸알미늄, talc. 人工腸液中에서는 magnesium trisilicate, kaolin, talc, 天然珪酸알미늄, aluminum hydroxide의 順이었다.

Magnesium stearate는 물과의 親和力이 없기에 berberine HCl 液과의 接觸이 不充分하여 전혀 吸着하지 않았다

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