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VIUSID
its effect on the production
of
interferon in experiment

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VIUSID, its effect on the production of interferon in experiment. *Khodjaev Sh.Kh., Saidkulov A.M.*

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The search for efficient, etiotropic drugs in particular, for treatment of patients with infectious diseases was and still is an urgent problem for research.

The fact that being the only causal factor in the formation of infectious process and being not decontaminated in the human organism for months and sometimes years, infectious agent can be the only drive in transition of a disease from acute to lingering and chronic form. Viral hepatitis B and C are the illustration for the fact.

The search for virusotropic drugs and, primarily, their study in experimental conditions is the demand of the times. In view of the above we were dealing with the study on effect of VIUSID on formation of interferon in experimental animals.

Methods. VIUSID was administered to not thoroughbred mice with weight of 10-12g in various doses (5-10-25-50-100 mg/kg). It was administered to the animals one, two and three times intraperitoneally, perorally, rectally and subcutaneously. For each dose of the preparation 5 mice were intended. Activity and time of interferon formation induction (in titers U/ml) in each experiment was studied in 4-12-24-48-72-144-168 hours after the preparation application. MEGOSIN, an inducer of interferon, possessing interferon-inducing activity and usually used in medical practice, was taken as the control for the experiment in similar mode and doses.

Formation of significantly high titer of endogenous interferon can be observed upon all ways of administration for VIUSID (Table 1). Its high interferon-inducing activity can be seen in rectal way of administration (1024 U/ml), what is valuable and suitable in clinical conditions, optimal interferon-inducing dose being 50 mg/kg. Upon intraperitoneal and peroral ways of administration interferon synthesis level was somewhat lower – 256-51 U/ml. Analysis of the dynamics of endogenous interferon accumulation in mice blood serum shows that interferon response to administration of one and the same dose of the inducer under study intraperitoneally and perorally is quite different (Fig.1). Rectal administration of VIUSID induced significant output of interferon, maximum levels of the latter in mice blood serum being registered in 24 hours (1024 U/ml) after administration. By 96 hours interferon titers significantly decreased.

When VIUSID is administered intraperitoneally, interferon induction starts earlier, than upon the rectal way of administration. Interferon titers in mice blood serum reach their maximum in 12 hours after induction. Maximum interferon induction upon peroral and subcutaneous ways of administration can

be observed in 48 hours after administration. Maximum interferon titers registered upon rectal administration of VIUSID were 2-4 times higher of those produced upon other ways of administration of the preparation.

Organism hyporeactivity with typically low production of interferon in response to the repeated administration of an inductor is known as one of the limitations to clinical usage of inductors. Its manifestation degree depends on a dose of an inductor, duration being determined by a type of animals and nature of inductor.

Inductors were administered to the animals three times with various intervals (2 and 2 days) between administrations. The second dose of preparation played role of a probe in determination of organism's capacity to induce interferon in response to repeated administration of the preparation (Fig.2). Multiple studies enabled us to establish that two-time administration of VIUSID revealed the progression of hyporeactivity on the 3rd day after its administration. The phenomenon can be noted within next 4 days (Fig.3). In 168 hours after the first administration the animals start going out of nonsusceptibility.

In view of the above, we made an attempt to design the regimen for multiple usage of VIUSID, that is, for prolonged effect of the preparation. It was established that one and the same inductor could be administered 2 times in a row with a 24- hour interval. Nonsusceptibility progresses and within first 144 hours causes stimulation of interferon production. Between the second and the third administration of the inductor it is necessary to make a 4-day pause, transiting on the nonsusceptibility phase, then the inductor can be administered 2 times with 24-hour interval, in response to what the organism starts producing high titer of interferon.

Nonsusceptibility of organism can be also overcome by a change of interferon inductor. Analysis of interferon induction dynamics showed that interferon response to one and the same dose of inductor administered by various ways was different.

Administration of VIUSID first intraperitoneally and in 48 hours perorally results in marked interferon production in response to repeated administration of the preparation (Fig. 4).

Analysis of the findings shows that hyporeactivity phenomenon is the complex one. Despite the fact, its overcoming is possible upon thorough working of the preparation administration regimens.

Study on VIUSID efficacy upon experimental murine hepatitis ("Mescherina" strain) in white not thoroughbred mice indicates that significantly high protection effects could be reached upon prophylactic administration of the preparation within 24 hours (40%) before infection. It should be mentioned that upon intraperitoneal administration of VIUSID, in contrast to MEGOSIN, protection of animals has been observed not only upon prophylactic regimen, but also upon the therapeutic one. Maximum protection of infected animals was observed upon administration of the inductor not only in 4 hours after infection (40%), high protection effect (45%) being seen upon its administration in 24 hours after infection.

VIUSID can be concluded to possess interferon-inducing activity.

Table. 1^a Comparative study on interferon-inducing activity of viusid with the one of megosin, interferon inductor

№ п/ п	Preparation	Dose of mg/kg	Way of administration	Interferon activity (u/ml)
1	VIUSID	5 10 25 50 100	Intraperitoneally	32-64 64 128 256-512 256-512
	Megosin	5 10 25 50 100		8-16 16 16-32 32-64 32-64 128-256

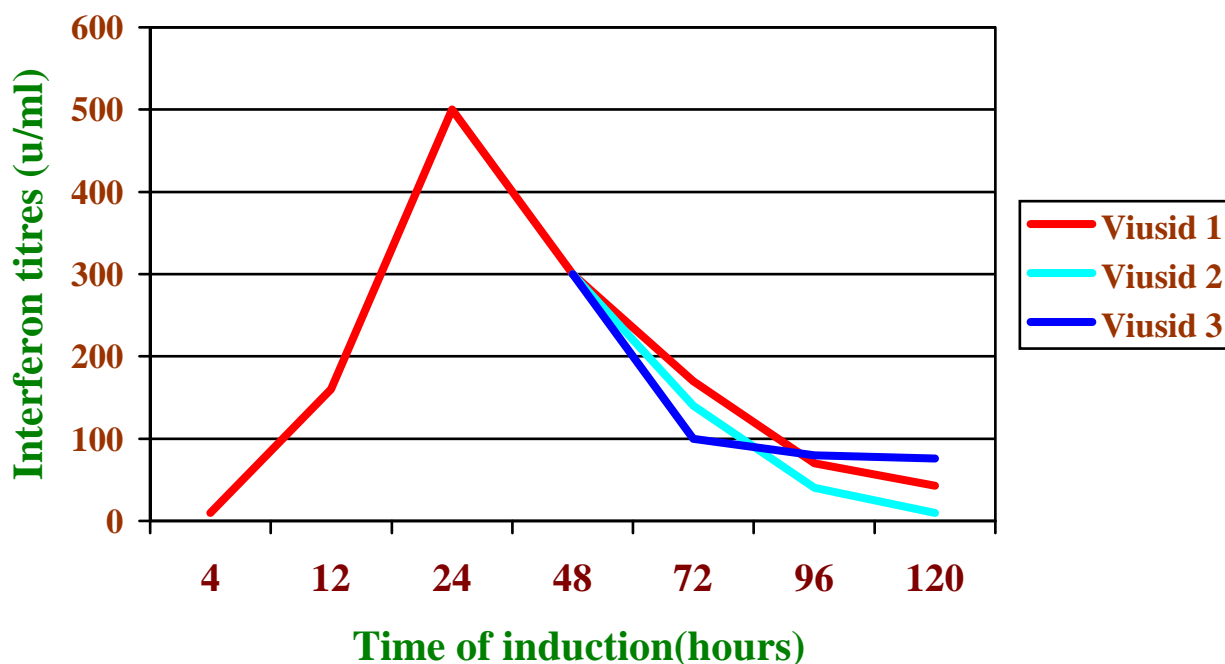
Table. 1b

№ п /	Preparation	Dose (mg/kg)	Way of administr ation	Interferon activity, (u/ml)
2	VIUSID	5 10 25 50 100	Per orally	<4 16-32 32 256-512 256-512
	Megosin	5 10 25 50 100		<4 4-8 32-64 64-128 64-128

Table. 1c

№ п / п	Prepara tion	Dose of mg/kg	Way of adminis- tration	Interferon activity, u/ml.
3	VIUSID	5 10 25 50 100	Rectally	64-128 128-256 256 512 512
	Megosin	5 10 25 50 100		16-32 32-64 80-160 160 320

Interferon production in experimental animals as a response to one time (1), two time(2) and three time(3)per oral administration of "VIUSID"



Anti-viral activity of viusid in experimental animals in the murine viral hepatitis "Mischerina strain"

Nº	Preparation	Time of administration in relation to infection, hours	Animal survival rate (%)	Protection effect (%)	Mean life time (days)	Đ
1	Megosin	-24	40	30	6.9	<0.05
		-4	30	20	5.2	>0.05
		+4	35	25	6.4	>0.05
		+24	40	30	7.5	<0.05

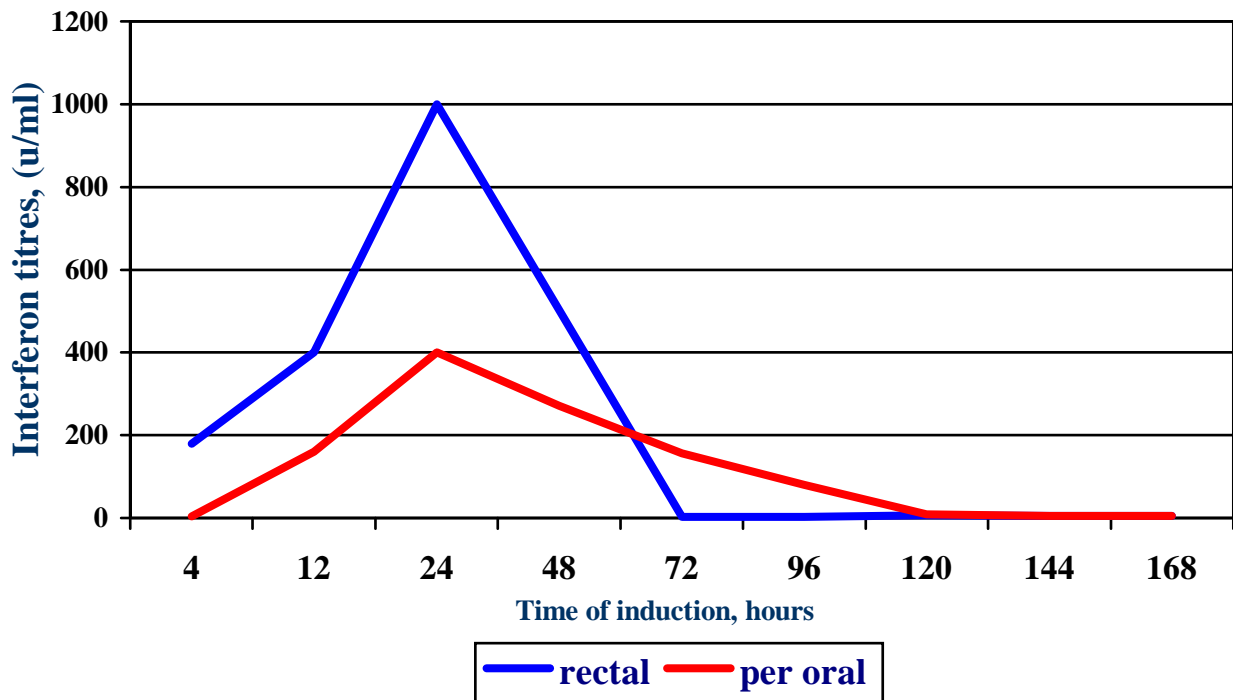
Note: 20 not thoroughbred mice with mean weight of 10-20 g were taken for every experiment

Continuation

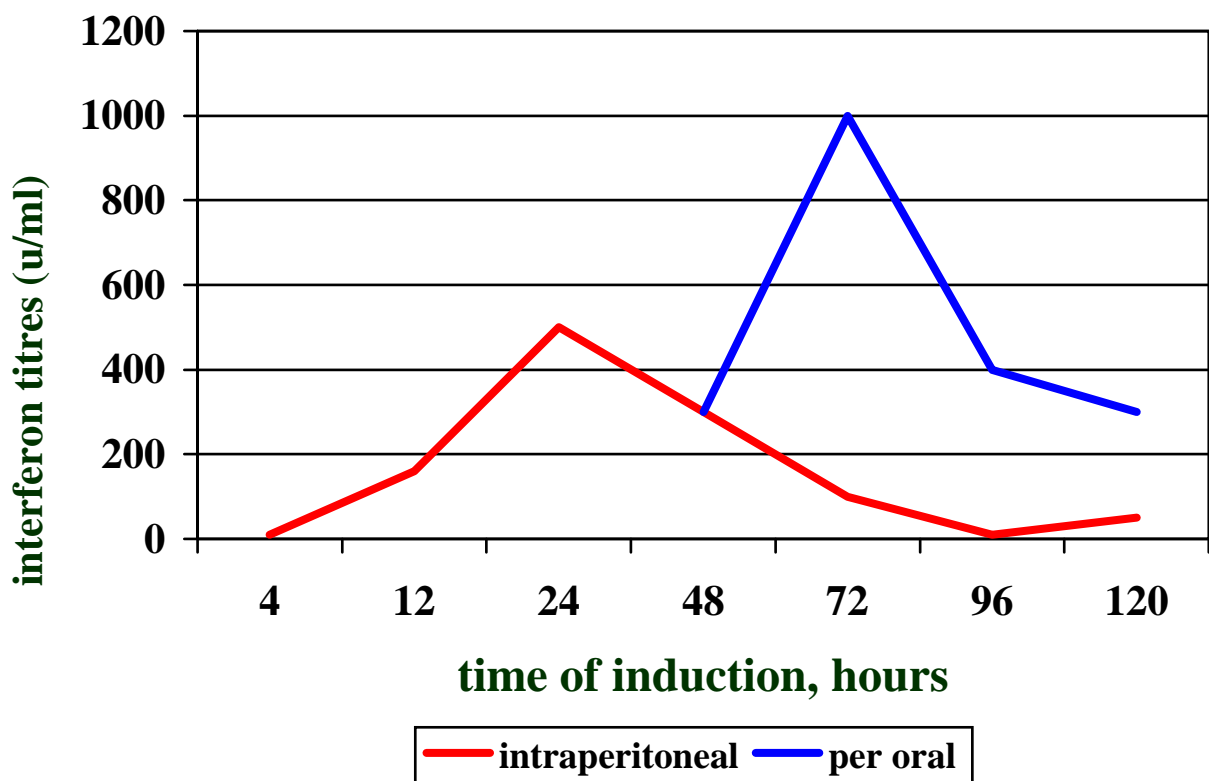
Nº	Prepara- tion	Time of administrati on in relation to infection (Hours)	Animal survival rate (%)	Protec- tion effect (%)	Mean life time (days)	P
2	VIUSID	-24 -4 +4 +24	50 40 50 55	40 30 40 45	8.1 7.8 8.2 8.4	<0.01 <0.05 <0.01 <0.01

Note: 20 not thoroughbred mice with mean weight of 10-20 g were taken for every experiment

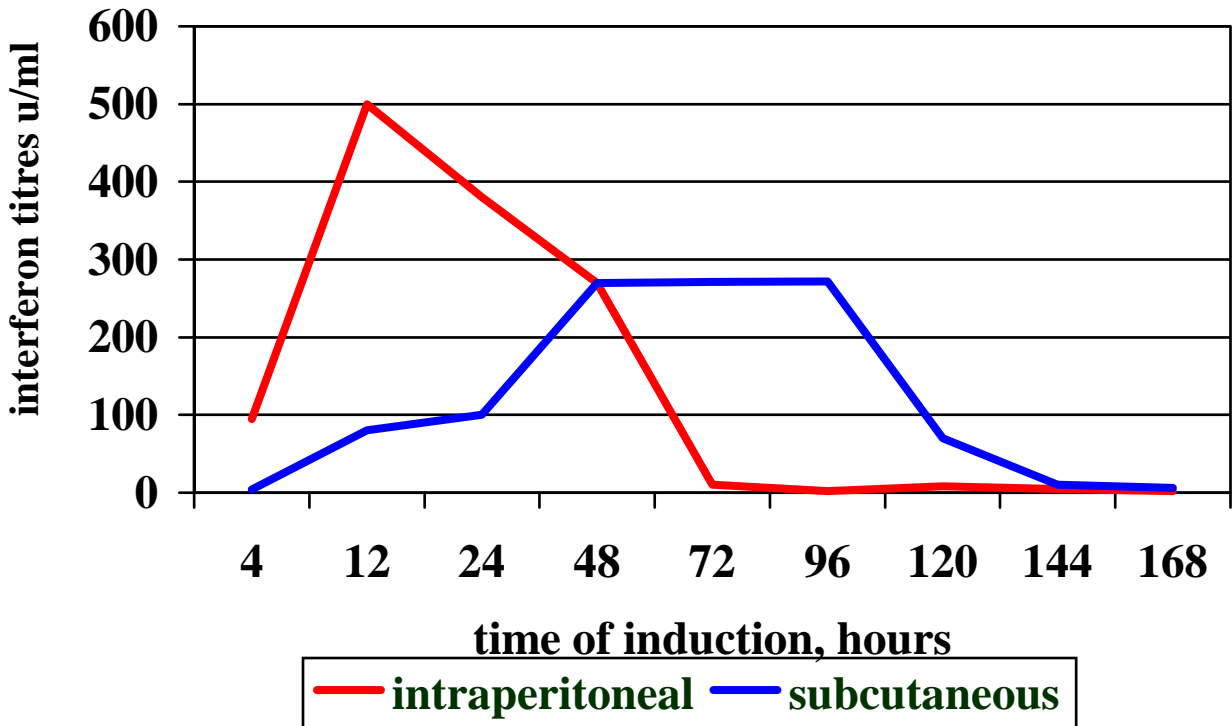
Interferon induction in experimental animals, administered with "Viusid"



Interferon production in experimental animals administered with "Viusid" intraperitoneally (1) and per orally (in 48 hours)



Interferon induction in animals administered with "Viusid"



Interferon production in response to one time(1) and repeated(2) Administration of "Viusid" to experimental animals, one-time Per orally administration of "Megosin"(3) and rectal administration of "Viusid"(4)

