Clinical Trial of a Hepatoprotective Compound* in Acute Viral Hepatitis and in the Patients of Tuberculosis Receiving ATT

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Viral hepatitis may be defined as a systemic viral infection marked by hepatic cell necrosis and hepatic inflammation which leads to characteristic clinical, biochemical and histologic changes. It is a major health problem throughout the world affecting several hundreds of millions of persons every year. It is also responsible for considerable morbidity and mortality both from acute infection and from its chronic sequelae. Several oral antitubercular drugs can cause hepatitis and hence the rationale for a hepatoprotective drug along this treatment.

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Material and methods

Patients were selected from O.P.D. and Indoor of Kayachikitsa Deptt. of S.S. Hospital, Institute of Medical Sciences, Banaras Hindu University, Varanasi. The acute viral hepatitis was established on clinical and biochemical grounds. Anorexia, nausea, vomiting, malaise, fever, tenderness in right hypochondriac region with hepatomegaly were the criteria for clinical diagnosis. The biochemical criteria was serum levels of bilirubin, SGOT, SGPT and serum level of alkaline phosphatase. Patients suffering from clinical illness for more than 7 days receiving some other drug or with history of the use of hepatotoxic drugs were excluded from the study.

Patients satisfying the inclusion criteria were allotted to group I (Trial group) and group II (Control) comprising of fifty and twenty patients respectively. The patients of group I were treated with hepatoprotective compound (Amlycure DS) the composition of which is given in Table 1 and placebo was given to patients of group II.

The tubercular patients selected for the study were also divided into group IIIrd and IVth comprising of fifty patients in each group. The patients of group IIIrd (Trial group) were treated with antitubercular treatment (Isonex, Rifampicin,

Table 1.

Composition of Amlycure DS Each 10 ml of syrup contains aqueous extracts of			
Kasni	600 mg	Gokhru	70 mg
Birangasif	20 mg	Sharphunka	120 mg
Jhau	20 mg	Kasondi	20 mg
Makoi	80 mg	Haritaki	300 mg
Pitpapra	300 mg	Bhringraj	750 mg
Bhuiamla	750 mg	Raktapunernava*	550 mg
Kutki	100 mg	Kalmegh	100 mg
Arjuna	35 mg	Guduchi	200 mg
Rasaunt	20 mg	Amla	20 mg
Chitrak	150 mg	Vidang	150 mg
Raktrohida	150 mg	Kalipath	150 mg
Kurchi	200 mg	Nishoth	150 mg
Daruharidra	150 mg	Tulsi	30 mg
and		Moolishar	50 mg
Sugar base	q.s.		

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** The Hepatoprotective Compound used in the trial was Amlycure DS, courtesy Aimil Pharmaceuticals (INDIA) Ltd.*

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Table 2.

Pre and post treatment severity scores of symptoms and signs

		Before treatment		After treatment							
		0		4th day		7th day		14th day		21st day	
		Control	Trial	Control	Trial	Control	Trial	Control	Trial	Control	Trial
Anore-xia	x	1.85	2.12	1.80	1.50	1.20	0.98	0.8	0.34	0.55	0.10
	±SD	0.75	0.72	0.61	0.41	0.41	0.59	0.41	0.52	0.51	0.30
	±SE	0.17	0.10	0.09	0.09	0.08	0.08	0.09	0.07	0.11	0.04
	t	-	-	0.27	3.50	0.55	8.70	5.90	14.21	6.50	18.36
	p	-	-	>0.05	>0.05	<0.01	<0.001	<0.001	<0.001	<0.001	<0.001
Malaise	x	1.75	1.64	1.95	1.34	1.35	0.74	0.35	0.34	0.95	0.10
	±SD	0.72	0.60	0.22	0.56	0.49	0.63	0.49	0.52	0.39	0.30
	±SE	0.16	0.08	0.05	0.07	0.11	0.08	0.11	0.07	0.09	0.04
	t	-	-	1.20	2.05	2.08	6.94	4.50	11.07	7.40	15.70
	p	-	-	>0.05	<0.05	<0.05	<0.001	<0.001	<0.001	<0.001	<0.001
Nausea	x	1.55	1.38	1.60	1.02	0.85	0.56	0.60	0.18	0.25	-
	±SD	0.60	0.69	0.50	0.65	0.36	0.57	0.11	0.38	0.44	-
	±SE	0.14	0.09	0.11	0.09	0.08	0.08	0.11	0.05	0.09	-
	t	-	-	0.29	3.89	4.45	6.40	5.49	10.70	7.83	-
	p	-	-	>0.05	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	-
Vomiting	x	1.30	0.88	1.00	0.54	0.80	0.18	0.50	-	0.20	-
	±SD	0.47	0.74	0.73	0.57	0.69	0.38	0.51	-	0.41	
	±SE	0.11	0.10	0.16	0.08	0.16	0.54	0.11	-	0.09	
	t	-	-	1.60	2.56	2.70	5.90	5.20	-	7.90	
	p	-	-	>0.05	<0.05	<0.01	<0.001	<0.001		<0.001	
Pain abdomen	x	1.40	1.24	1.45	0.90	0.9	0.36	0.65	0.12	0.03	0.02
	±SD	0.50	0.62	0.60	0.46	0.56	0.48	0.50	0.32	0.50	0.14
	±SE	0.11	0.08	0.14	0.07	0.12	0.07	0.11	0.04	0.11	0.02
	t	-	-	2.80	3.10	3.01	3.20	4.80	11.3	7.20	11.20
	p	-	-	>0.05	<0.01	<0.01	<0.01	<0.01	<0.001	<0.001	<0.001
Icterus	x	1.35	1.88	0.75	1.36	1.25	0.76	0.75	0.26	0.55	0.18
	±SD	0.48	0.77	0.44	0.72	0.64	0.71	0.44	0.48	0.51	0.38
	±SE	0.11	0.11	0.09	0.10	0.14	0.10	0.09	0.06	0.11	0.05
	t	-	-	2.70	3.60	0.57	7.80	4.20	13.20	5.30	14.[illegible]
	p	-	-	>0.05	<0.001	<0.05	<0.001	<0.001	<0.001	<0.001	<0.001
Tenderness	x	1.30	0.28	0.45	0.96	1.05	0.50	0.75	0.22	0.50	0.02
	±SD	0.47	0.64	0.68	0.64	0.68	0.58	0.47	0.42	0.51	0.14
	±SE	0.11	0.09	0.15	0.09	0.15	0.08	0.11	0.05	0.11	0.02
	t	-	-	0.81	2.50	1.40	6.40	4.10	0.80	5.20	13.70
	p	-	-	>0.05	<0.05	>0.05	<0.001	<0.001	<0.001	<0.001	<0.001
Liver size	x	1.10	1.02	1.30	0.72	1.10	0.34	0.50	0.08	0.45	-
	±SD	0.64	0.82	0.73	0.60	0.72	0.47	0.51	0.27	0.51	-
	±SE	0.43	0.12	0.16	0.08	0.16	0.07	0.11	0.04	0.11	-
	t	-	-	0.93	2.10	0.00	5.10	3.33	7.70	3.60	-
	p	-	-	>0.05	<0.05	>0.05	<0.001	<0.001	<0.001	<0.01	-
Mean morbidity score		11.6	11.40	12.30	8.40	8.50	4.42	4.85	1.54	3.75	0.42

Pyrazinamide and Ethambutol) and hepatoprotective compound drug. The patients in group IVth received antitubercular treatment only.

Hepatoprotective drug (Amlycure DS) was administered in the dose of 2 teaspoon full thrice daily for 3 weeks in the cases of acute viral hepatitis and for 4 months in cases of tubercular patients. Similar instructions about dietary habits were given to the patients of acute viral hepatitis of both the groups.

Assessment of patients

Patients suffering from viral hepatitis were evaluated basally at the time of first visit and followed up on day 4th, 7th, 14th and 21st of the treatment. Clinical signs and symptoms were graded on a scale from 0 to 3 (0-absent, 1-mild, 2-moderate and 3-severe). Biochemical investigations were done initially and on 4th, 7th, 14th and 21st day of the treatment. The effect of trial drug was assesed by reduction in the severity of the clinical signs and symptoms and by reduction in the values of serum bilirubin, alkaline phosphatase and serum transaminases.

In tubercular patients, liver function test was done initially and at monthly intervals for 4 months in both the groups to observe the biochemical changes.

The hepatoprotective drug has favourable influence on the severity and course of illness in the patients of acute viral hepatitis and in the patients suffering from tuberculosis. Rapid decline in biochemical parameters in the cases of viral hepatitis suggests the utility of this drug in reducing the morbidity.

Results

Mean reductions in serum bilirubin, SGOT, SGPT and alkaline phosphatase were significantly higher in the trial group as compared to control in the cases of acute viral hepatitis. There was progressive improvement in biochemical values and symptoms from the first follow up onwards, while in control group at the time of first followup the mean values were higher than the basal. Out of the five HBsAg positive patients, one

Table 3 (a).

Pre and post treatment statistical values of biochemical investigations

		Before treatment		After treatment							
		0		4th day		7th day		14th day		21st day	
		Control	Trial	Control	Trial	Control	Trial	Control	Trial	Control	Trial
Se. Bil.	x	5.95	9.26	7.19	7.46	5.60	5.35	4.20	3.51	3.30	1.83
	± SD	1.80	5.23	2.10	4.52	1.60	3.66	1.60	2.44	1.33	1.15
	± SE	0.40	0.74	0.50	0.64	0.35	0.51	0.35	0.34	0.30	0.16
	t	-	-	2.02	1.84	3.40	4.30	3.40	5.30	0.54	9.80
	p	-	-	<0.05	>0.05	<0.05	<0.001	<0.01	<0.001	<0.001	<0.001
Se. Alk. Phos.	x	20.95	20.07	20.55	16.42	17.65	14.54	14.00	12.92	12.70	11.20
	± SD	3.60	5.02	3.80	4.07	3.70	2.96	2.59	2.23	1.90	1.59
	± SE	0.80	0.71	0.86	0.57	0.80	0.41	0.58	0.31	0.43	0.22
	t	-	-	0.34	3.98	2.80	6.70	6.75	9.20	8.80	11.90
	p	-	-	>0.05	<0.001	<0.01	<0.001	<0.001	<0.001	<0.001	<0.001
SGOT	x	162.5	285.19	157.90	191.60	109.20	125.50	80.20	74.40	56.40	51.80
	± SD	82.8	353.40	61.40	282.10	30.70	187.70	13.60	58.80	9.10	19.20
	± SE	18.5	49.90	13.70	39.90	6.90	26.60	3.04	8.30	2.03	2.70
	t	-	-	0.20	1.50	2.70	2.80	4.40	4.20	5.70	4.70
	p	-	-	>0.05	>0.05	<0.05	<0.01	<0.001	<0.001	<0.001	<0.001
SGPT	x	205.1	356.30	184.10	218.70	132.4	141.60	85.90	116.80	64.30	52.60
	± SD	108.3	449.90	116.70	278.40	73.4	222.20	18.90	278.90	18.90	19.05
	± SE	24.2	62.03	26.10	39.40	16.4	31.40	4.30	39.50	4.20	2.70
	t	-	-	0.60	1.90	2.5	1.1	4.90	4.60	5.87	4.90
	p	-	-	>0.05	>0.05	<0.05	>0.05	<0.001	<0.001	<0.001	<0.001

patient from the treated group also cleared the antigen.

Group IIIrd patients having tuberculosis received A.T.T. with hepatoprotective drug and showed notable improvement in appetite. None of the patients of this group developed jaundice during the trial period. The SGOT and SGPT values were also within the normal range in this group. In the group IVth, four patients out of fifty developed icterus. SGOT and SGPT values were also on the higher side of normal range in most of the patients in this group. Nine patients out of fifty had increased value of serum transaminases (see Table 3 b).

Mean morbidity scores for clinical parameters showed significant reduction in trial group (Table 2). Most of the patients were relieved of anorexia, nausea, vomiting, malaise and liver tenderness at the end of 3rd week in the trial group. Mean score of icterus declined significantly in trial group. Improvement in signs and symptoms scores and biochemical values was much better in trial group in comparison to control group (see Table 3 a). No significant side effects were observed during the trial.

Table 3 (b).

Pre and post treatment statistical values of biochemical investigations in the tuberculosis patients.

		Trial group (ATT + Hepatoprotective drug)					Control group (ATT only)				
		Initial	Follow up				Initial	Follow up			
		0	Ist	2nd	3rd	4th	0	Ist	2nd	3rd	4th
Serum	x	0.7	0.78	0.84	0.73	0.77	0.73	0.98	0.79	0.73	0.71
Bili.	±SD	0.17	0.08	0.09	0.13	0.09	0.18	0.77	0.19	0.12	0.16
Alk.	X	9.60	10.78	11.08	10.68	10.10	10.20	10.50	10.60	13.50	10.92
Phos.	±SD	2.45	2.12	2.00	1.47	1.77	1.79	2.79	2.01	2.63	1.84
SGOT	x	36.46	34.86	34.10	37.38	35.26	34.93	35.14	36.76	36.48	37.90
	±SD	5.87	4.07	3.24	6.07	5.06	5.40	4.28	6.01	7.42	7.56
SGPT	x	40.80	39.74	37.64	37.30	34.24	36.02	41.18	44.14	45.32	44.40
	±SD	6.66	6.19	5.99	6.46	5.69	7.73	10.70	14.27	16.18	15.82

The hepatoprotective drug has favourable influence on the severity and course of illness in the patients of acute viral hepatitis and in the patients suffering from tuberculosis. Rapid decline in biochemical parameters in the cases of viral hepatitis suggests the utility of this drug in reducing the morbidity. Higher transaminases value in control group in comparison to trial group in the patients of tuberculosis suggests the hepatoprotective activity of the trial drug.

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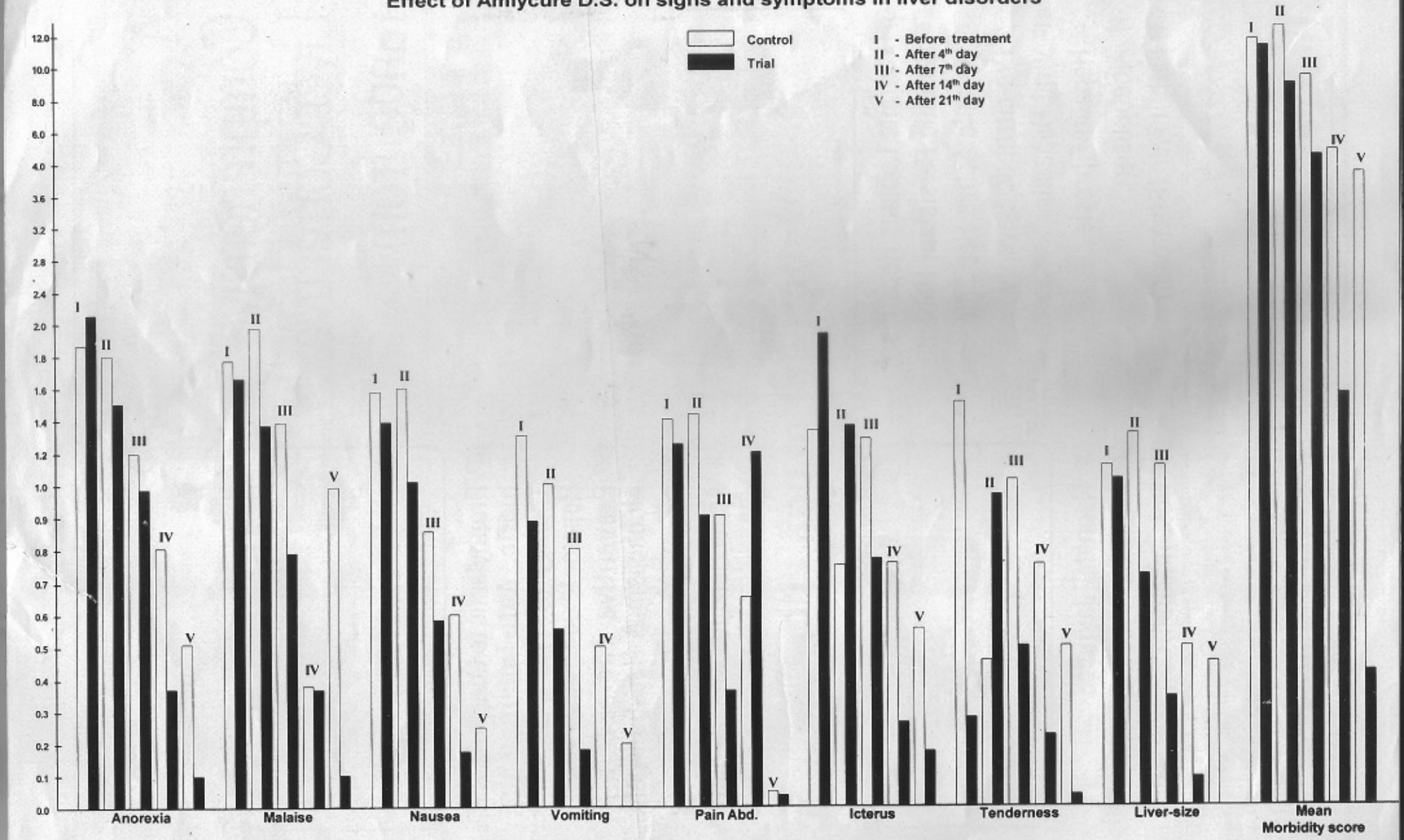
References

1. Sherlock S. Virus hepatitis in diseases of Liver Biliary system. 9th Ed.. Blackwell Scientific Publ.. Oxford 1989. pp 308.
2. Zuckerman AJ. The chronicle of viral hepatitis Bull. Hyg. Trop Dis. 1977;54:113.
3. Toshniwal NK. Yagnik VH. Panday KN. and Rabdiya MV. Clinical profile of viral hepatitis & study of 1569 cases. the Indian Practioner (1990. 43 (7) 567.
4. Mehrotra R. et al. Indian J. Med. 1990(B)92:133.
5. Thyagrajan SP. et al. The Lancet 1988: Oct 1. 864.
6. Antarkar DS. Vaidya AB. and Doshi JC. A double blind clinical trial of Arogya Vardhini in acute viral hepatitis. Ind J Med Res. 1982. 72. 588.
7. Dwivedi Y. et al. Ind J Med Res.. 1990(B)92:195.

Effect of Amlycure D.S. on signs and symptoms in liver disorders



Clinical sign scale:- 0 - Absent, 1 - Mild, 2 - Moderate, 3 - Severe

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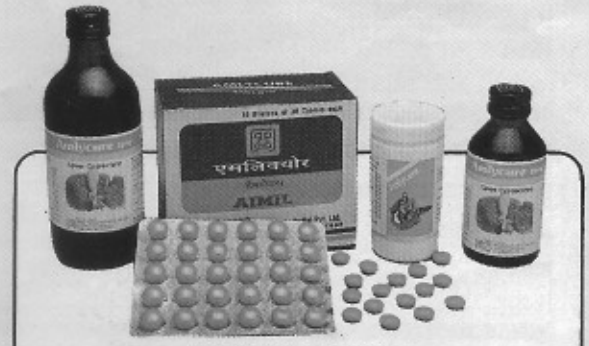

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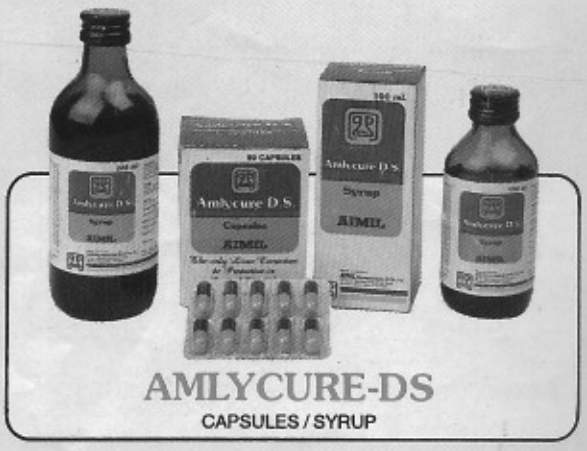

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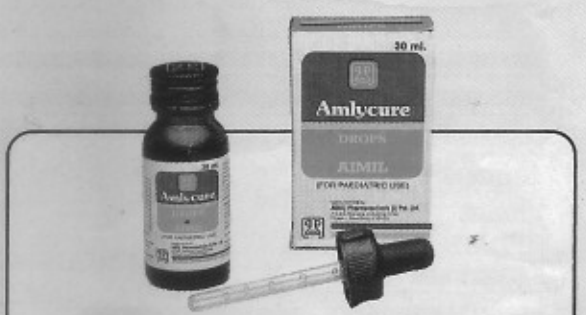

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