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HAZARD CHARACTERISTICS OF ISOSORBIDE DINITRATE—LACTOSE MIXTURES

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Summary

Attempts have been made to study the hazard potential of isosorbide dinitrate (ISDN) which is widely used in treatment of angina and hypertension. To permit safe handling, this compound is diluted with suitable inert excipients such as lactose, mannitol, etc. The ASTM Chemical Thermodynamic and Energy Release Evaluation program (CHETAH) was used to get an *a priori* knowledge of the hazard characteristics of ISDN—lactose mixtures. Pentaerythritol tetranitrate (PETN)—lactose system was chosen as the reference. The results indicate that while a PETN—lactose mixture in the ratio 20/80 could have a high hazard potential, mixtures of ISDN—lactose having ISDN content less than 40% should be safe. Experimental studies have been carried out on pure ISDN and its mixtures with lactose to investigate their thermal stability, impact and friction sensitivities, and sensitivity to initiation to detonation by standard No. 6 and No. 8 strength detonators. It has been found that although pure ISDN and ISDN—lactose mixtures have a poor thermal stability compared to PETN—lactose system, their friction, impact, and shock sensitivities are minimal. Strength measurements were also performed using lead block expansion and ballistic mortar techniques. It is concluded that ISDN—lactose mixtures have a low hazard potential.

Introduction

Isosorbide dinitrate (ISDN) is known to possess medicinal properties similar to pentaerythritol tetranitrate (PETN) and is widely used in angina and hypertension. ISDN, a white crystalline powder, is reported to be a powerful explosive and is, therefore, diluted with lactose, mannitol, or other suitable inert excipients to permit safe handling for pharmaceutical purposes [1]. Normally, the dilute blend contains approximately 25% ISDN and 75% lactose.

Physical and chemical properties:
Chemical name: 1,4;3,6-dianhydro-2,5-dinitrosorbitol
Molecular formula: $C_6H_8N_2O_8$
Molecular weight: 236.15
Aspect: explosive, white crystals
Melting point: 69°C—70°C

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Explosion temperature: 180°C—185°C
Abel's Heat Test: 1 hour at 60°C

Hazard evaluation by CHETAH program

Chemical Thermodynamic and Energy Release Evaulation program of ASTM was used to evaluate the hazard potential of pure ISDN, pure PETN and their mixtures with lactose [2]. The CHETAH program is useful for the prediction of the potential maximum reaction energy of chemical compounds and the results of the program provide an indication of relative sensitivity, and serve as a guide for further testing. The computed results are presented in Table 1.

The results of Table 1 lead to the following conclusions: pure ISDN has a high hazard potential. CHETAH predicts that while a ISDN/lactose mixture of the ratio 40/60 could have a high hazard potential, the PETN/lactose system in the ratio 30/70 might be hazardous.

TABLE 1

Hazard evaluation of ISDN-lactose and PETN-lactose systems

System	Ratio	ΔH_{decomp} (cal. g^{-1})		$\Delta H_{comp} - \Delta H_{decomp}$		Oxygen balance (g/100 g)		$Y = \Delta H^2 W/n$	
		Value	Rating	Value	Rating	Value	Rating	Value	Rating
ISDN	100	—1.23	H	—1.59	H	—54.2	H	149.2	H
Lactose	100	—0.46	M	—3.14	M	—106.6	H	15.8	L
ISDN/lactose	20/80	—0.60	M	—2.83	M	—96.1	M	28.3	L
ISDN/lactose	30/70	—0.68	M	—2.67	M	—90.9	H	37.1	M
ISDN/lactose	40/60	—0.76	H	—2.52	H	—85.6	H	47.5	M
ISDN/lactose	50/50	—0.84	H	—2.36	H	—80.4	H	59.5	M
ISDN/lactose	70/30	—0.99	H	—2.06	H	—69.9	H	89.0	M
PETN	100	—1.58	H	—0.30	H	—10.1	H	273.6	H
PETN/lactose	10/90	—0.57	M	—2.81	M	—95.5	H	25.4	L
PETN/lactose	20/80	—0.70	M	—2.49	M	—84.8	H	39.1	M
PETN/lactose	30/70	—0.82	H	—2.19	H	—74.5	H	56.0	M
PETN/lactose	50/50	—1.05	H	—1.61	H	—54.7	H	99.3	M
PETN/lactose	70/30	—1.27	H	—1.06	H	—36.1	H	156.3	H

Key: H — High; M — Medium; L — Low; W — weight of the compound; n — number of moles.

Experimental and results

Sample preparation

Crude ISDN was recrystallised from acetone/water mixture to obtain pure ISDN. The required quantities of ISDN and lactose were mixed in a polyethylene bag and sieved through BSS 52 mesh to ensure uniform particle size distribution of ISDN in all the samples.

PETN/lactose samples were also prepared in the same manner as described above. Care was taken to keep the particle size distribution of PETN similar to that of ISDN.

Thermal stability — DSC studies

Thermal stability studies of ISDN, ISDN/lactose (30/70) mixture and PETN/lactose (30/70) mixture were conducted using a differential scanning calorimeter (DSC), Perkin-Elmer Model DSC-1B(3). The temperatures at which various peaks were observed are given in Table 2.

The results of Table 2 show that ISDN decomposes at a lower temperature than PETN. Moreover, the thermogram of ISDN also shows small exothermic peaks around 180°C, indicating the onset of decomposition. On the other hand, it was found that ISDN/lactose and PETN/lactose mixtures, both in the ratio of 30/70, have similar decomposition patterns; the decomposition of the mixtures being mostly endothermic and requiring temperatures in excess of 300°C for completion. This reveals the large desensitising effect of lactose on the thermal decomposition pattern of the pure highly reactive ingredients, PETN and ISDN.

TABLE 2

DSC studies on ISDN-lactose system

System	Nature of peak	Maximum peak temperature (°C)	Remarks
1. ISDN	Endo.	72	Melting of ISDN.
	Exo.	223	Sharp peak denoting rapid decomposition.
2. Lactose	Endo.	325	Broad endotherm indicating slow decomposition.
3. ISDN/lactose (30/70)	Endo.	79	Melting of ISDN.
	Endo.	199	Decomposition of ISDN/lactose mixture.
	Endo.	212	
	Exo.	223	
	Endo.	327	
4. PETN	Endo.	140	Melting of PETN.
		230	Sharp peak denoting rapid decomposition.
5. PETN/lactose			Similar to ISDN/lactose mixture except for the endotherm due to the melting of PETN around 140°C.

Impact and friction sensitivity studies

Impact and friction sensitivity of ISDN and PETN were determined by the conventional Fall-hammer and Julius—Peter techniques [4]. The results are presented in Tables 3 and 4.

The results in Tables 3 and 4 unambiguously establish that ISDN and its 20% lactose formulation are insensitive to impact and friction, even though PETN/lactose (20/80) formulation is impact sensitive.

TABLE 3

Test No.	Sample*	Weight (kg)	Height (cm)	Remarks (% samples fired)
1.	PETN	2	50	20
			60	50
			70	80
2.	PETN/lactose (20/80)	2	70	20
			80	40
			90	80
3.	ISDN	5	200	Nil
4.	ISDN/lactose (20/80)	5	200	Nil

*Weight — 5 mg.

TABLE 4

Friction sensitivity data

Test No.	Sample	Load (kg)	Result (% samples fired)
1.	PETN	16.8	20
		19.2	80
2.	PETN/lactose (20/80)	36.0	Nil
3.	ISDN	36.0	Nil
4.	ISDN/lactose (20/80)	36.0	Nil

Cap sensitivity test

Cap sensitivity test provides a simple means for identifying whether a material is sensitive to standard No.6/No.8 strength detonator. If the sample is initiated to detonation, the material is classified as an explosive, otherwise, as a blasting agent.

ISDN and PETN samples diluted with various percentages of lactose were examined for their cap sensitivity. The samples were filled into kraft paper cartridges of 20, 25 and 32 mm diameter. A standard No.6/No.8 blasting cap was inserted into the cartridge which was then placed on soft ground. The detonator was then fired and it was observed whether a crater formed. The sample was considered to be cap-sensitive if a crater was formed. The results of these studies are given in Table 5.

From the results obtained on the initiation sensitivity of ISDN/lactose and PETN/lactose mixtures, we arrived at the following conclusions:

I. ISDN/lactose mixtures having an ISDN content in the range 10—50% are insensitive to both No.6 and No.8 detonators. In our attempts to measure the

TABLE 5

Initiation sensitivity of ISDN/lactose and PETN/lactose mixtures

Test No.	System	Ratio	Charge diameter (mm)	Type of detonator	Result
1.	ISDN/lactose	30/70	32	No.8	NI
2.		40/60	32	No.8	NI
3.		50/50	32	No.8	NI
4.	PETN/lactose	20/80	20	No.8	NI
5.		20/80	25	No.6	Partial detonation
6.		20/80	32	No.6	I
7.		30/70	20	No.8	I
8.		30/70	20	No.6	I
9.		30/70	25	No.6	I

Key: I — Initiated; NI — not initiated.

ballistic-mortar-weight strength of ISDN/lactose mixtures, we observed that a 50/50 mixture did not give any deflection (except for the contribution of the detonator), whilst a 75/25 ISDN/lactose mixture was cap-sensitive.

II. PETN/lactose mixtures could be initiated to detonation even in 20 mm diameter when the PETN percentage was 30% and more.

III. Comparison of the above initiation sensitivity results definitely establishes that ISDN/lactose mixtures possess far lower shock sensitivity in comparison to PETN/lactose system.

TABLE 6

Strength values for ISDN-PETN-lactose systems

	Sample	Ballistic mortar weight strength (%)	Lead block expansion value (ml)	Remarks
1.	ISDN	64.6*	304	
2.	ISDN(75)/lactose(25)	42.5	212	
3.	ISDN(50)/lactose(50)	No deflection	11	The composition is non-cap-sensitive
4.	PETN	100.0	521	
5.	PETN(75)/lactose(25)	69.7	362	
6.	PETN(50)/lactose(50)	48.5	207	
7.	PETN(40)/lactose(60)	41.4	135	

*SG 80 = 80% (Reference).

Strength measurements

In order to have a knowledge of the strength of the ISDN/lactose and PETN/lactose mixtures, ballistic mortar and lead block expansion techniques were utilized. A 10-g sample was used for both tests and aluminium foil was used as a wrapper for ballistic mortar determination [5]. The values obtained are given in Table 6.

The results of Table 6 show that ISDN/lactose mixtures up to 50% ISDN have no explosive properties.

Conclusions

The present study encompasses precariousness, sensitivity and strength measurements on pure isosorbide dinitrate and its mixtures with lactose. PETN/lactose served as the reference system.

The results clearly indicate that:

- pure isosorbide dinitrate possesses minimal impact and friction sensitivities though its thermal stability is poor. Pure ISDN and its mixtures with lactose are sensitive to No.6 detonator only if the ISDN content is more than 60%.
- The corresponding mixtures based on PETN appear to be more sensitive than those based on ISDN, which is to be expected, since PETN is known to be a powerful high explosive.
- ISDN/lactose formulation in the ratio 25/75 which is used for medicinal purposes has a very low hazard potential and is safe for handling.

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