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Research Article

Formulation and Evaluation of Amlodipine Immediate Release Tablet

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Abstract: The purpose of this research is to prepare amlodipine immediate release tablets by direct compretion method. In order to obtain the best, optimized product four different formulations were developed. Different super disintegrants, binding agents and lubricant were taken as variables. Weight variation, thickness, hardness, friability, disintegration time, in-vitro release and pharmaceutical assay were studied as response variables. Capping was observed in formulation containing PVP K-30.The formulation F4 was selected as optimized formulation. The different physical properties and in-vitro release profile showed best results with the reference product.
Keywords: Amlodipine, anti-hypertensive, immediate release, super disintegrants.

INTRODUCTION

An immediate release dosage form allows a manufacturer to extend market exclusively, while offering patients a convenient dosage form or dosage regimen. Immediate Release Tablets are those tablets which are designed to disintegrate and release their medication with no special rate controlling features, such as special coating and other techniques **[**1].

Recently immediate release tablets have started gaining popularity and acceptance as a drug delivery system, mainly because they are easy to administer, has quick onset of action is economical and lead to better patient compliance. They are also a tool for expanding market, extending product life cycles and generating opportunities. Immediate release tablets have advantages like they are economical and cost effective, quick onset of action, suitable for industrial production, improved stability and bioavailability, adaptable and amendable to existing processing and packaging machinery and unique product differentiation. While bears the disadvantages like rapid drug therapy intervention is not possible, some times may require more frequency of administration, dose dumping may occur, reduced potential for accurate dose adjustment.

Disintegrants are substances or mixture of substances added to the drug formulation that facilitates the breakup or disintegration of tablet or capsule content into smaller particles that dissolve more rapidly than in the absence of disintegrants. Superdisintegrants are generally used at a low level in the solid dosage form. ideal properties of disintegrants include poor solubility, poor gel formation, good hydration capacity, good molding and flow properties, no tendency to form complexes with the drugs [2].

Amlodipine is an antihypertensive drug having Chemical Formula $C_{20}H_{25}ClN_2O_5$, weight 408.876 and protein binding: 97.5%. It is hepatically metabolized extensively (90%) to inactive metabolites via the cytochrome P450 with a half life of about 30-50 hours and has bioavailability 64-90% [3].

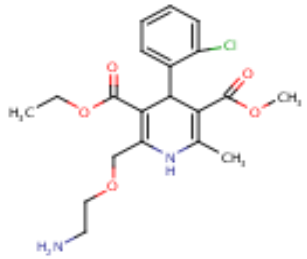

Fig.1: Chemical structure of amlodipine

The presented study was aimed to formulate and evaluate the immediate release tablets of amlodipine using the excipients microcrystalline cellulose (Functional category: adsorbent; suspending agent, diluents, tablet disintegrant), AC-DI-SOL [croscarmellose sodium](Functional category: adsorbent tablet and capsule disintegrant), lactose (Functional category: Adsorbent Tablet and capsule diluent, diluents for dry power inhalers), polyvinylpyrrolidone (Functional category: adsorbent disintegrant; dissolution aid; suspending agent; tablet binder), aerosil (Functional category: Adsorbent Adsorbent; anticaking agent; emulsion stabilizer; glidant; suspending agent; tablet disintegrant; thermal stabilizer; viscosity-increasing agent), magnesium stearate (Functional Category: Tablet and capsule lubricant) [4, 5] .

METHOD

Preformulation study [6, 7]

Angle of Repose (□)

The friction forces in a loose powder can be measured by the angle of repose (□). It is an indicative of the flow properties of the powder.It is defined as

maximum angle possible between the surface of the pile of powder and the horizontal plane.

tan (□)= h / r

□ = tan^{-1} (h / r)

Where, □ is the angle of repose.

h is the height in cms r is the radius in cms.

The powder mixture was allowed to flow through the funnel fixed to a stand at definite height (h). The angle of repose was then calculated by measuring the height and radius of the heap of powder formed. Care was taken to see that the powder particals slip and roll over each other through the sides of the funnel.

Bulk Density (Db)

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weight powder (passed through standard sieve # 20) into a measuring cylinder and initial weight was noted. This initial volume is called the bulk volume. From this the bulk density is calculated according to the formula mentioned below. It is expressed in g/ml and is given by

Db = M / Vb

Where, M is the mass of powder

Vb is the bulk volume of the powder.

Tapped Density (Dt)

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 100 times and the tapped volume was noted if the difference between these two volumes is less than 2%. If it is more than 2%, tapping is continued for 12-50 times and tapped volume was noted. Tapping was continued until the difference between successive volumes is less than 2 % (in a bulk density apparatus). It is expressed in g/ml and is given by

Dt = M / Vt

Where, M is the mass of powder

Vt is the tapped volume of the powder.

Carr's index (or) % compressibility

It indicates powder flow properties. It is expressed in percentage and is given by

I = Dt – Db / Dt X 100

Where,

Dt is the tapped density of the powder ,

Db is the bulk density of the powder.

Hausner's ratio

Hausner's ratio is an indirect index of ease of powder flow. It is calculated by the following formula.

Hausner's ratio = Dt / Db

Where, Dt is the tapped density

Db is the bulk density.

Lower hausner's ratio (<1.25) indicates better flow properties than higher ones (>1.25).

Post formulation study [6, 7]

Weight variation

20 tablets were selected randomly from the batch and weighed individually to check for weight variation. Weight Variation Specification is as per IP. % Deviation for 80 mg or less ±10, more than 80 mg but less than 250 mg ±7.5, 250 mg or more ±5.

Hardness (or) tablet crushing strength (fc)

Hardness or tablet crushing strength (fc) (the force required to break a tablet in a diametric compression) was measured using Monsanto tablet hardness tester . It is expressed in kg/cm^2.

Thickness

The thickness of the tablets was measured using vernier caliber. It is expressed in mm.

Friability (F)

Friability of the tablet determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at I height of 6 inches in each revolution. Pre weighted sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were de dusted using a soft muslin cloth and reweighed. The friability (F) is given by the formula.

$F = W_{initial} - W_{final} / W_{initial} * 100$

***In-vitro* Dissolution Study**

The test for *in vitro* drug release studies are usually carried out in simulated gastric and intestinal fluids maintained at 37^{o}C. In practice, IR time is determined by using the USP dissolution apparatus containing 900ml of 0.1N HCl as a testing medium maintained at 37^{o}C. The time required to IR dosage form is noted as immediate release time. Dissolution tests are performed using the USP dissolution apparatus. Samples are withdrawn periodically from the dissolution medium, replenished with the same volume of fresh medium each time, and then analyzed for their drug contents after an appropriate dilution. Recent methodology as described in USP XXIII states that the dosage unit is allowed to sink to the bottom of the vessel before rotation of blade is started. A small, loose piece of non reactive material such as not more than a few turns of wire helix may be attached to the dosage units that would otherwise IR. However, standard dissolution methods based on the USP or British Pharmacopoeia (BP) have been shown to be poor predictors of *in vitro* performance for immediate releasing dosage forms.

Formulation of Amlodipine immediate release tablets [8, 9]

Amlodipine immediate release tablets by using direct compression method. The drug and all other excipients were sifted through #40 sieves and mixed thoroughly. To above blend was pre lubricated with aerosil and

lubricated with magnesium stearate. The above lubricated blend was compressed using standard flat faced punch on a sixteen station rotary tablet punching machine.

Table 1: Composition of formulations

Formulation/ Ingredients	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)
Amlodipine	5	5	5	5
Microcrystalline cellulose	66.8	65.8	64.8	63.8
Lactose	20	20	20	20
Polyvinyl pyrolidine	5	5	5	5
Crascarmellose sodium	2	3	4	5
Aerosil	0.6	0.6	0.6	0.6
Mg.stearate	0.6	0.6	0.6	0.6
Total	100	100	100	100

RESULTS:

UV spectrophotometric method was developed for the amlodipine. The method obeys beer's low in the concentration of 5-25 µg/ml with regression coefficient of 0.999. Thus the said method was found to be suitable for the estimation of amlodipine in In-vitro dissolution studies at λmax 237nm.

Table 2: Data for standard calibration curve of Amlodipine in 0.1N HCl

Sl. No	Concentration(µg/ml)	Absorbance(nm)
1	0	0
2	5	0.132
3	10	0.281
4	15	0.421
5	20	0.552
6	25	0.687

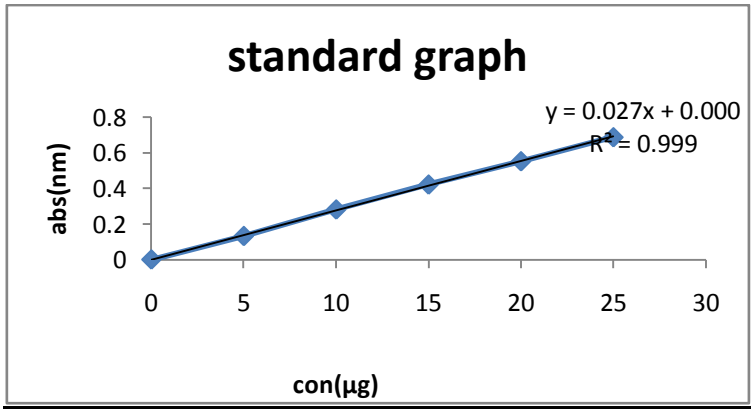

Fig. 2: Standard calibration curve of Amlodipine in 0.1N HCl

Table 3: Preformulation studies data for Amlodipine immediate release tablet

Formulation code/ Parameters	Bulk density (g/cc)	Tapped density(g/cc)	Angle of Repose	Carr's index	Hausner's ratio
F1	0.446	0.56	25.74	20.35	1.25
F2	0.48	0.637	24.28	24.6	1.32
F3	0.478	0.586	26.06	18.43	1.22
F4	0.469	0.561	27.4	16.39	1.19

The weight variation of all the formulations was within the range. The drug content of Amlodipine from all the formulations was found in the range of 99% to 100%. The hardness was constantly maintained 3.0kg/cm^2 during compression. Friability for all the formulation shown less than 0.15% which is in the acceptable limits which indicates formulations have good mechanical strength.

Table 4: Post formulation studies data for Amlodipine immediate release tablet

Formulation code/ Parameters	Hardness (kg/cm^2)	Friability (%)	Disintegration time (sec)	Content uniformity	Weight variation
F1	3.0	0.15%	26	99.4%	99±2
F2	3.1	0.12%	22	99.90%	99±3
F3	3.0	0.11%	18	99.36%	99±2
F4	3.0	0.10%	15	99.94%	99±1

Formulation 1 was prepared using microcrystalline cellulose 66.8% and crosscarmellose sodium 2% in concentration, PVP K 30 as diluent. These are punched using 6mm punch, having 100 mg tablet weight. It was evaluated for In-vitro dissolution studies.

Table 5: *In-vitro* dissolution data for Amlodipine immediate release tablet (F1)

Sl. No.	Time(min)	% CDR	%to be released	Log % to be released
1	5	46	54	1.73
2	10	61	39	1.59
3	15	73	27	1.43
4	30	89	11	1.04
5	45	96	04	0.6

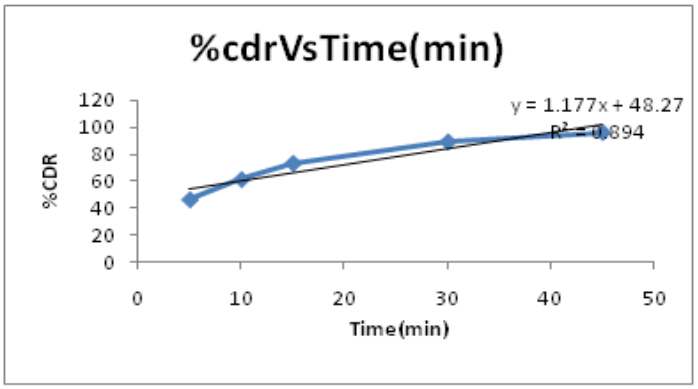

Fig. 3: Cumulative % drug release (CDR) Vs Time plot showing *in-vitro* release of Amlodipine from F1 in 0.1 N HCl

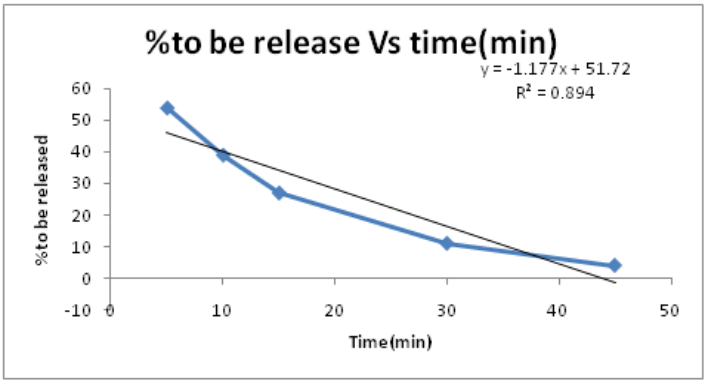

Fig. 4: % to be released Vs Time plot showing *in-vitro* release of Amlodipine from F1 in 0.1 N HCl

Formulation 2 was prepared using microcrystalline cellulose 65.8% and cross carmellose sodium 3% in concentration, PVP K 30 as diluent. These are punched using 6mm punch, having 100 mg tablet weight. These are evaluated for In-vitro dissolution studies.

Table 6: In-vitro dissolution data for Amlodipine immediate release tablet (F2)

Sl.No.	Time(min)	% CDR	%to be release	Log % to be released
1	5	54	56	1.74
2	10	69	31	1.5
3	15	82	18	1.3
4	30	90	10	1
5	45	98	02	0.3

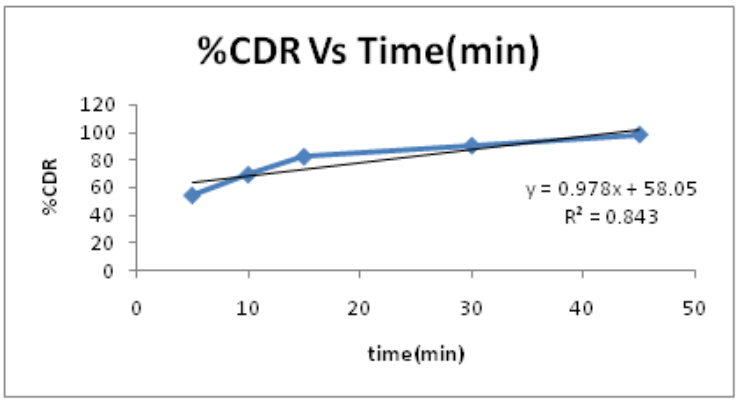

Fig. 5: Cumulative % drug release (CDR) Vs Time plot showing *in-vitro* release of Amlodipine from F2 in 0.1 N HCl

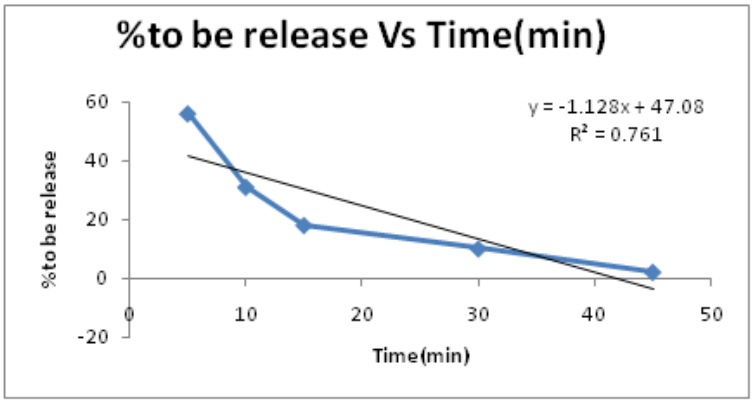

Fig. 6: % to be released Vs Time plot showing *in-vitro* release of Amlodipine from F2 in 0.1 N HCl

Formulation 3 was prepared using microcrystalline cellulose 64.8% and crosscarmellose sodium 4% in concentration, PVP K 30 as diluent. These are punched using 6mm punch, having 100 mg tablet weight. These are evaluated for In-vitro dissolution studies.

Table 7: *In-vitro* dissolution data for Amlodipine immediate release tablet (F3)

Sl. No:	Time(min)	% CDR	%to be released	Log % to be released
1	5	61	39	1.59
2	10	74	26	1.41
3	15	82	18	1.25
4	30	98	02	0.30

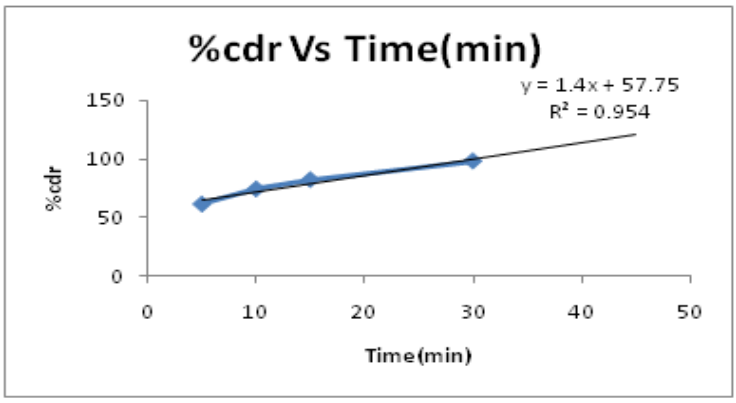

Fig. 7: Cumulative % drug release (CDR) Vs Time plot showing *in-vitro* release of Amlodipine from F3 in 0.1 N HCl

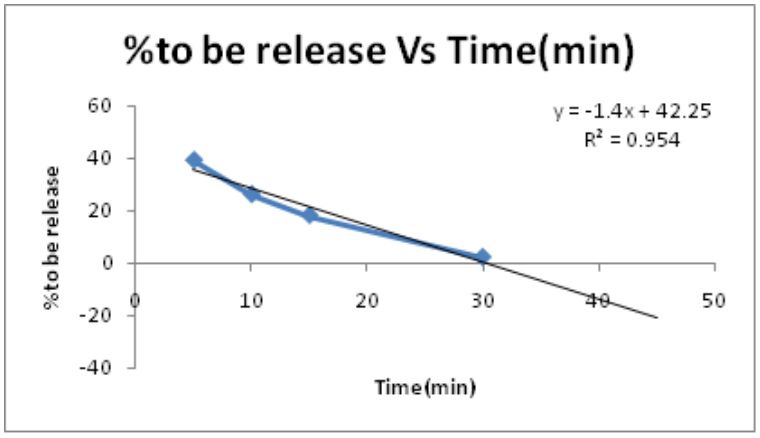

Figure 8: % to be released Vs Time plot showing *in-vitro* release of Amlodipine from F3 in 0.1 N HCl

Formulation 4 was prepared using microcrystalline cellulose 63.8% and cross carmellose sodium 5% in concentration, PVP K 30 as diluent. These are punched using 6mm punch, having 100 mg tablet weight. These are evaluated for In-vitro dissolution studies.

Table 8: In-vitro dissolution data for Amlodipine immidiate release tablet (F4)

Sl.No	Time(min)	% CDR	% to be released	Log % to be released
1	5	72	28	1.44
2	10	86	14	1.14
3	15	98	02	0.30
4	30	-	-	-
5	45	-	-	-

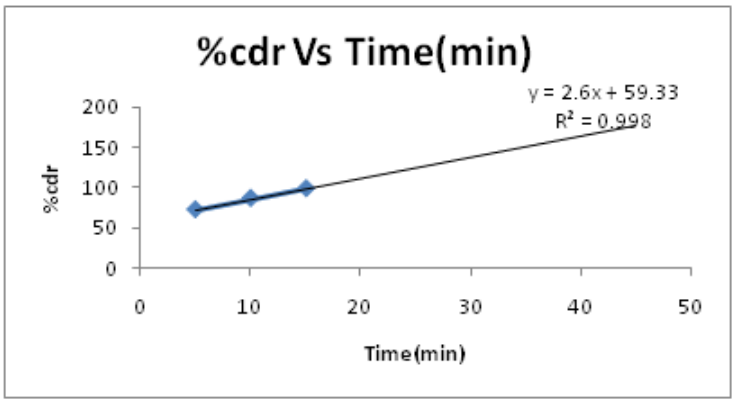

Fig. 9: Cumulative % drug release (CDR) Vs Time plot showing *in-vitro* release of Amlodipine from F4 in 0.1 N HCl

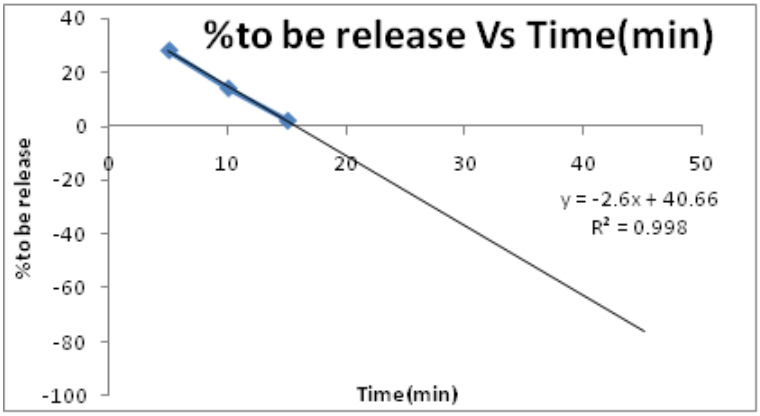

Fig. 10: % to be released Vs Time plot showing *in-vitro* release of Amlodipine from F4 in 0.1 N HCl

Table 9: Comparative of % CDR & DT of F1, F2, F3 and F4 for amlodipine immediate release tablets

Formulation cod/time in min	5	10	15	30	45	Disintegration time (sec)
F1(%)	46	61	73	89	96	26
F2(%)	54	69	82	90	98	22
F3(%)	61	74	82	98		18
F4(%)	72	86	98			15

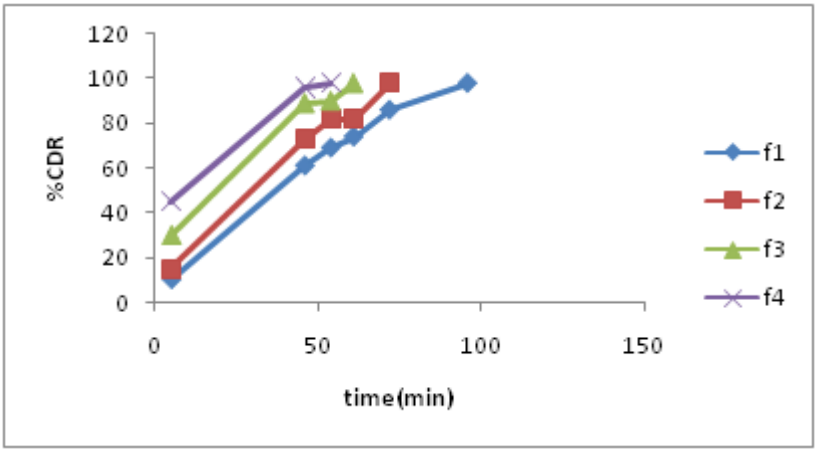

Fig. 11: comparative of % CDR Vs time (min) of F1, F2, F3 and F4 for amlodipine

Invitro dissolution test were conducted for all the formulation from F1,F2,F3&F4 in 0.1 HCl. 96% & 98% of the drug was found to be released at the end of 45 min from F1& F2 respectively. 98% of the drug was found to be released at the end of 30 min from F3. 98% of the drug was found to be released at the end of 15 min from F4.

The promising formulations, the formulation F4 emerged as the overall best formulation based on drug release characteristics, which showed 98% release of drug in 15 min. The main evaluation for an IR tablets is the *in vitro* dispersion time or disintegration time which was found to be the least (15 sec) for F4 formulation, When compared to remaining formulations.

CONCLUSSION

All formulations were formulated with microcrystalline and cross carmellose sodium at concentrations 4,5,7.5% respectively. Among the promising formulations, the formulation F4 emerged as the overall best formulation based on drug release characteristics, which showed 98% release of drug in 30 min. The main evaluation for an IR tablets is the in-vitro dispersion time or disintegration time which was found to be the least (15 sec) for F4 formulation. When compared to F1, which showed an *in vitro* dispersion time of disintegration time of 26 sec.

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