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RESEARCH ARTICLE

FORMULATION AND EVALUATION OF THYROID HORMONE(T3) IMMEDIATE RELEASE TABLETS

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Abstract

The study was aimed to formulate and evaluate Thyroid hormone (T3) immediate release tablets of a model Reference Listed Drug (RLD). The objective was to develop a cost effective immediate release tablet formulation and to optimize the formula in product development same that of the reference product. The ingredients used were API (thyroid hormone), lactose monohydrate (diluent), acacia (binder), maize starch (disintegrant), sodium chloride (alkalinizing agent) and magnesium stearate (lubricant). The concentration of maize starch and magnesium stearate were altered to reach the objective. Totally five formulations (F1 - F5) were prepared by direct compression method. The plan of work involved involved in the study was[1] Selection of drug and excipients, [2]Physico–chemical characterization and drug identification, [3]Preformulation parameters of the drug, [4]Pre–compression parameters for the tablet blend, [5]Formulation and development of the tablet dosage form, [6]Post compression parameters of the tablet and [7]Stability study. The stability studies were performed as per ICH guidelines. Among all the formulations F5 was found to be the best as it showed better results than the other formulations. In vitro disintegration time and percentage drug release results shown satisfactory results. Stability study results showed no significant changes in the formulation.

Keywords: Thyroid hormone (T3), Immediate release tablets, Direct compression, Dissolution.

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Introduction

Tablets are the most popular and easiest way of drug administration for the patients. Compared to other dosage forms tablets are easy to prepare and dispense.(1) Mostly preferred route of administration of drug is oral route and this route is widely used for new and existing drugs. It is due to its ease of administration and most impotantly patient compliance. (2) Solid oral delivery systems do not require sterile conditions and are therefore, less expensive to manufacture.(3) Solid orals incudes tablets, capsules and other dosage forms that are taken by mouth. Immediate release tablets are those which disintegrate rapidly and get dissolved to release the medicaments.(4) Immediate release medications work quickly just as their name suggests. The onset of action for the immediate release tablets will be fast once they enter the system . The advantage is that they start working quickly but the relief does not last longer than a few hours.(5) Most of the thyroid hormones are given as solid orals. There are two types of thyroid hormones. Thyroxine (T4) and Triiodothyronine (T3) are the two main types of thyroid homones secreted by thyroid gland.. T3 is the active form of thyroid hormone. It is most commonly used to treat hypothyroidism and myxedema coma. (6) Some of the thyroid drugs in the market are cytomel, synthroid, proloid, armour thyroid, bitiron.

Materials and Methods

Materials :

Liothyronine sodium (Azico biophore), Lactose monohydrate (DFE Pharm), Acacia (Spectrum), Maize starch (Roquette), Sodium chloride (FMC Biopolymer), Magnesium stearate (Peter Grevens) and quantity was taken as in Table no.1. All the materials and reagents were of analytical grade.

Methodology

Physico-chemical characterisation of the drug: This refers to the physical description, partition coefficient and pH determination.

Preformulation parameters study of the drug: The drug was checked for loss on drying to determine its water and volatile substances by using moisture anlayzer. Solubility study was evaluated in various physiological pH media (1.2, 4.5 and 10). Drug and excipient compatibility study was done to check the interaction between the API and the excipients.

Pre – compression parameters study for the tablet blend: It was done to check the flow properties of the tablet blend. This includes bulk density, tapped density, compressibility index, hausner ratio and angle of repose.

Formulation and development stages: All the drug and the excipients were dispensed. API, sodium chlorde, acacia and maize starch were sifted through 100# separately. Lactose and magnesium stearate were sifted through 40# and 60#. All were mixed except lactose. The mixed blend was loaded in the blender and lactosed was added as three equal parts separately. Sifted magnesium stearate was added to the above blend mix and lubricated in the blender. Prepared blend was compressed under 16 station compression machine.

Post compression parameters of the tablet: The tablets were compressed and checked for post compression parameters like weight variation test, thickness, hardness, friability, disintegration, dissolution, assay and content uniformity.

Stability study: Tablets are loaded for the stability determination at Accelerated Stability Condition (40°C/75%RH). After the specific time (1 month) it is taken and tested for pH, assay, RS, content uniformity, water content, disintegration, dissolution and description. All these parameters are compared with the initial sample and also checked whether it complies with specifications and only if it complies with specifications the batch will pass the test.

Results and discussion

Physico-chemical characterisation of the drug:

White or slightly coloured, hygroscopic odourless powder.

Partition coefficient:

The partition coefficient of the drug at 25°C for 24 h was found to be 1.04. Therefore, it is confirmed that the drug is practically insoluble in water. Hypothetically, it is assumed it has higher permeability in GI tract.

pH determination of drug:

Determination of pH was carried out in 1 %w/v drug dispersion, and the reported value was 7.1.

Pre - formulation parameters study of the drug :

Loss on Drying :

The LOD was found to be 1.2% and found in line with standard range of LOD. The sample is less likely to absorb moisture which does not have any impact on stability issue related to moisture and shall be considered as safe to expose in high humid condition during process development.

Solubility study :

Highest solubility was seen in pH 10 with alkaline borate buffer with 0.31 mg/ml. Hence alkaline borate buffer with pH 10 was opted as release media for the dissolution study of the finished product.

Drug & excipient compatibility study:

From the results given in Table no.2, it is confirmed that no extra peaks were observed in physical mixture and can be concluded that all the excipients are compatible with API. Hence, it was found that excipients don't have interaction with API.

Pre – compression parameters study for the tablet blend:

From the Table no.3, it was found that compressibility index and hausner's ratio are within the range of good flow property. Hence, direct compression is opted.

Assay:

The assay of the drug in F5 formulation was found to be 101%. The values for the formulations are within the limits. F5 exhibited much closer assay valve to the RLD.

Content Uniformity:

The content uniformity in formulation (F5) was found to be AV 13, which is within the specification limit (NMT AV 15). F5 exhibited much closer content uniformity value to the RLD.

Dissolution:

The dissolution profile for the study formulations F1-F5 exhibits release percentage of falling within the limits at 30 min. Thus, based on the similarity factor for the formulations F1-F5 in comparison to RLD it was observed that formulations F1, F2, F3 & F4 exhibited a comparable amount of percentage release difference from the RLD value, whereas F5 formulation showed a much closer release profile value as shown in fig. no 1 & 2.

Stability study:

From the results as in Table no. 5, there is no significant changes observed and found that all the parameters are within the limit and are stable.

. **Table No 1: Formulation table**

Ingredients	Mg/ tab				
Liothyronine sodium	0.02	0.02	0.02	0.02	0.02
Lactose Monohydrate	71.28	70.28	71.78	69.78	70.78
Acacia	2	2	2	2	2
Maize starch	5	5	4	6	5
Sodium chloride	1.2	1.2	1.2	1.2	1.2
Magnesium Stearate	0.5	1.5	1	1	1
Total weight	80mg	80 mg	80 mg	80mg	80 mg

Table No 2: Dec study result

Sample ID	Room temperature (RT)				40°C/75%RH			
	Colour change	Physical change	Assay	RS	Colour change	Physical change	Assay	RS
1	No	No	101.1	0.131	No	No	101.3	0.130
2	No	No	101.8	0.125	No	No	101.5	0.135
3	No	No	101.9	0.134	No	No	101.5	0.131
4	No	No	101.2	0.138	No	No	101.3	0.134
5	No	No	101.3	0.125	No	No	101.7	0.125
6	No	No	101.7	0.138	No	No	101.2	0.133
7	No	No	101.1	0.128	No	No	101.3	0.131

Table No 3: Pre – Compression parameters study result

Formulation Code	Bulk density (g/ml)	Tapped Density (g/ml)	Compressibility Index (%)	Hausner's ratio	Angle of Repose
F1	0.442	0.52	12	1.17	27.4
F2	0.441	0.50	13	1.13	28.5
F3	0.451	0 .52	13.2	1.15	28.3
F4	0.430	0.49	13.8	1.13	29.2
F5	0.431	0.51	12.8	1.18	26.1

Table No 4: Post compression parameters study result

Formulation	Average weight (mg)	Thickness (mm)	Hardness (N)	Friability %	DT(Mins)
F1	81	3.10	22	0.16	1'99"
F2	80.7	3.08	23	0.15	2'07"
F3	80.8	3.07	23	0.18	2'63"
F4	81	3.18	25	0.15	2'11"
F5	80.5	3.13	24	0.18	2'27"
RLD	80	3.14	24	0.19	2'30"

Table No 5: Stability study result

S.No	Tests	Limits	Initial	1st Month (40±2°C/75±5% RH)
1	**Description**	White, round shape, breakline on one side &GS on another side.	White, round shape, breakline on one side &GS on another side.	White, round shape, breakline on one side &GS on another side.
2	**Dissolution (% Drug Release)**	NLT 70% (Q) of Product is dissolved in 30 minutes.	95%	91%
3	**Assay**	90.0% to 110.0%	101.1%	100.8 %
4	**Content uniformity**	(NMT 15%)	13%	13%
5	**Related Substance**			
	Impurity A	NMT 1.0%	0.295%	0.298%
	Impurity B	NMT 1.0%	0.306%	0.322%
	Single max	NMT 1.0%	0.324%	0.347%
	Total Impurity	NMT 3.0%	0.185%	0.199%

Table No 6: Comparison of optimized formulation with reference product

S. No	Parameters	Reference Product	Optimized formulation
1	Appearance	White	White
2	Individual weight (± 10 % 72 mg to 88 mg)	80.00 mg	80.05 mg
3	Thickness	3.07mm,3.14mm	3.13mm
4	Hardness	24 N	24N
5	Disintegration time	2’ 30 Sec	2’ 27 sec
6	Dissolution (NLT 70% at 30 min)	95% release at 30min	94% release at 30min
7	Assay **(%) (**90.0 – 110.0)	103%	101%
8	Content Uniformity	12%	13%

Fig. No 1: Drug release profile

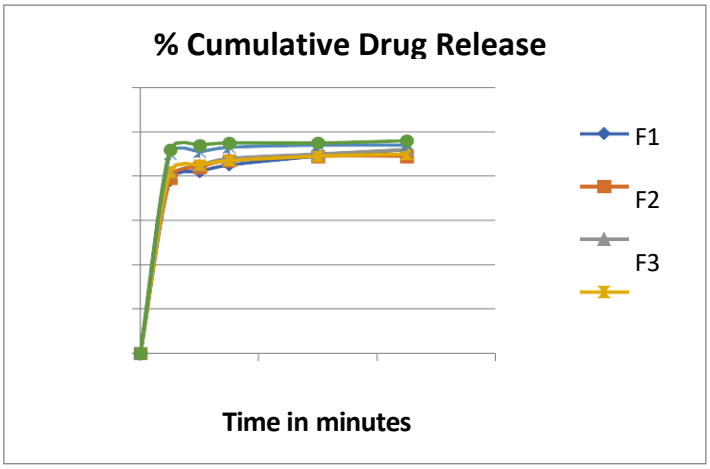
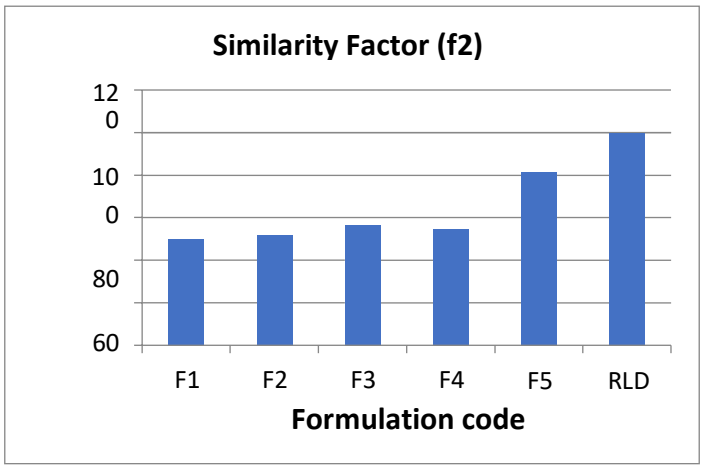


Fig. No 2: Similarity factor



Conclusion

RLD was selected and the parameters were checked for the formulation development. API and the excipients were chosen for five different formulations (F1 to F5) and the preformulation studies were done. After passing the pre-formulation studies, post-compression parameters and stability study were checked.

After comparing all the data obtained from the formulations (F1 to F5) with the RLD data, F5 formulation with 81% similarity factor was chosen as optimized formulation and short term stability study was carried out for one month period at room temperature and 40±2°C/75±5% RH. The results were found to be satisfactory within the specification limit.

Thus on the basis of research findings it was concluded that F5 formulation is the optimized formula when compared with the RLD.

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