Available online at http://www.advancedscientificjournal.com
http://www.krishmapublication.com
IJMASRI, Vol. 2, issue 1, pp. 389- 393, Jan. -2022
https://doi.org/10.53633/ijmasri.2022.2.1.001

INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY ADVANCED SCIENTIFIC RESEARCH AND INNOVATION (IJMASRI)

ISSN: 2582-9130 **IBI IMPACT FACTOR 1.5** **DOI: 10.53633/IJMASRI**

RESEARCH ARTICLE

FORMULATION AND EVALUATION OF THYROID HORMONE (T4) IMMEDIATE RELEASE TABLETS

Madhivardhana P*, Rajalakshmi A N, Padmapriya S

[1]*PG Student, Department of Pharmaceutics, Mother Theresa Post Graduate & Research Institute of Health Sciences, Puducherry.*

[2]*HOD, Department of Pharmaceutics, Mother Theresa Post Graduate & Research Institute of Health Sciences, Puducherry.*

[3]*Assistant Professor, Department of Pharmaceutics, Mother Theresa Post Graduate & Research Institute of Health Sciences, Puducherry..*

Abstract

The aim of this research work is to formulate and evaluate Levothroxine sodium immediate release tablets prepared by direct compression method . Five formulations were evaluated for different pre and post compression parameter and *in vitro* drug release studies.The results of pre compression parameters of formluation 1 to 5 were compared with prescribed limits. It showed that formulation 1 to 5 powder blend exhibit good flow property and compressibility property. The disintegration time of all formulation was found to be in the range 2mins 09 secsto 4mins 03 secs.Thus, based on evaluation of different parameters it was concluded that formulation of immediate release tablet Levothyroxine sodium was successfully done and F-5 showed almost 93% drug release at 45 mins in Alkaline borate buffer(pH 10).

Keywords: Thyroid hormone (T4), Immediate release tablets, Direct compression, Dissolution.

Corresponding Author:
Madhivardhana P
PG Student, Department of Pharmaceutics, Mother Theresa Post Graduate & Research Institute of Health Sciences, Puducherry
Mail: *vardhana1011@gmail.com*

Introduction

For drugs with a longer biological half-life, high bioavailability, reduced clearance, and lower elimination half-life, immediate release drug administration is desirable (Patel 2010).Immediate release drug delivery system is also conventional type

of drug delivery system designed to disintegrate and release medicaments with no special rate controlling features such as special coatings and other techniques. Immediate release drug delivery system are designed to give a fast onset of drug action (Schwartz 2000). Levothyroxine is a synthetically prepared levo-isomer of the thyroid hormone thyroxine (T_4, a tetra-iodinated tyrosine derivative) that acts as a replacement in deficiency syndromes such as hypothyroidism (Collier *et al*., 2011; Collier *et al*., 2010) [3,4].T_4 is the major hormone secreted from the thyroid gland and is chemically identical to the naturally secreted T_4: it increases metabolic rate, decreases thyroid-stimulating hormone (TSH) production from the anterior lobe of the pituitary gland, and, in peripheral tissues, is converted to T_3. Thyroxine is released from its precursor protein thyroglobulin through proteolysis and secreted into the blood where is it then peripherally deiodinated to form triiodothyronine (T_3) which exerts a broad spectrum of stimulatory effects on cell metabolism.

The plan of present research is the formulation choosen forLevothyrixine sodium immediate release tablet in order increase therapeutic efficacy in the treatment of hyperthyroidism and elegance with an added advantage of quick onset of action

Materials and Methods

Microcrystalline cellulose (DFE Pharm), Acacia (Spectrum), Maize starch (Roquette), Sodium citrate (FMC Biopolymer), Magnesium Stearate(Peter Grevens).

Preparation of immediate release levothyroxine sodium tablet

Immediate release tablets of were prepared by Direct compression method according to the formula given in Table 1. Levothyroxine sodium, acacia & maize starch were sifted through 100# separately. MCC (102) and magnesium stearate were sifted through 40 # and 60# mesh. All were mixed well except Magnesium stearate). Thoroughly mixed in a Rapid Mixer Granulator (RMG) for 10 min. The dried granules were blended in a blender for 5 min. Above mixer was lubricated for 5 min with Magnesium Stearate which was already passed through sieve No. 60. The lubricated granules were then compressed in to tablets on a 16 station rotary machine to get a tablet of 120 mg weight.

Pre compression parameter (Patrick J Sinko 2011; Lachman *et al.*, 2018)

The Precompression parameters were the primary requirements to determine whether the specific material was suitable for the targeted formulation or not. The various officially required pre compression parameters to be identified were bulk density, tapped density, Carr's index, Hausner's ratio and angle of repose for dosage form formulation.

Post compression parameter:

1) Thickness:

The thicknesses of the tablets were determined using electronic or digital Vernier'scaliper. Average thickness was calculated by measuring thickness of 10 tablets and it is determined in mm.

2) Hardness:

Hardness of the tablets was determined by Monsanto hardness tester. The average hardness was calculated by measuring hardness of 10 tablets and expressed in N or kg/cm^2.

3) Friability:

10 tablets were placed in the Roche friabilatorand the apparatus was rotated at a speed of 25rpm for 4 minutes (100 revolutions). The tablets were dedusted and reweighed. The percentage friability was calculated using the following formula.

$$\% \text{ friability} = \frac{W_0 - W}{W_0} \quad 100$$

4) Disintegration time:

The disintegration test was performed on six tablets using disintegration test apparatus in DM

water maintained at 37˚C in 900 ml. The device is allowed to travel up and down at a frequency of 28 to 32 cycles per minute, over a distance of 5 to 6 cm. Time taken to disintegrate the tablets completely was noted.

5) Weight variation test:

20 tablets were weighed individually and average weight was calculated, and the individual weight was compared with average weight. The difference in weight was determined and % variation was calculated.

6) *In vitro* Dissolution test:

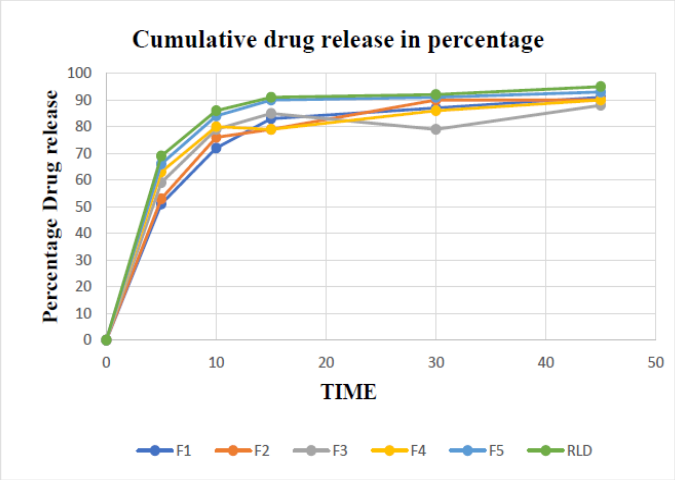

Fig. No 1: cumulative drug release in percentage

Dissolution study is performed using USP paddle apparatus. Study is carried out at 37°C temperature at 45 mins. At various time intervals, 5 ml sample is withdrawn and is replaced with same amount of Alkaline borate buffer (pH 10)

From the dissolution profile, it was found that all the formulations(F1 –F5) pass the dissolution test and exhibits the dissolution limit NLT 70% (Q) at 45 mins.; as given in figure 1.

Result and discussion

The result of pre compression parameters was summarized in Table 4. Angle of repose and Carr's index of formulation 1 to 5 compared with prescribed limits. It showed that formulation 1 to 5 powder blend exhibit good flow property and compressibility property.

The result of post compression parameters was summarized in Table 5. All the formulation showed uniform thickness. All the formulation got uniform hardness which was in the acceptable range. The normal acceptable criterion for friability is not more than 1.0%. Among the prepared formulation F-5 showed release rate of Levothyroxine sodium 93% at 45 mins.From above result, the formulation 5 was found to be optimized batch for further work

Table 1: Formula for preparation of immediate release levothyroxine sodium tablets

Ingredients	F1	F2	F3	F4	F5
	mg/ tab				
API	0.100	0.100	0.100	0.100	0.100
Microcyrstalinecellulose	71.9	76.9	78.1	79.4	79.9
Acacia	2.00	2.00	1.500	1.500	1.00
Maize starch	40.0	35.00	35.00	34.40	34.40
Sodium citrate	5.00	5.00	4.500	4.00	4.00
Magnesium Stearate	1.00	1.00	0.80	0.600	0.600
Total weight	120.00 mg	120.00 mg	120.00 mg	120.00 mg	120.00 mg

Table 2: Weight variation specification as per IP

Average Weight of Tablet	% Deviation
80 mg or less	±10
More than 80 mg but less than 250 mg	±7.5
More than 250	±5

Table 3: Result of pre compression parameter of formulation 1-5

Formulation Code	Bulk density	Tapped Density	Compressibility Index (%)	Hausner's ratio	Angle of Repose
F1	0.510	0.310	12	1.10	30.1
F2	0.512	0.331	13	1.12	31.2
F3	0.520	0 .344	13	1.14	32.2
F4	0.530	0.359	13.8	1.15	33.9
F5	0.536	0.364	14	1.16	33.1

Table 4: Result of post compression parameter of formulation 1-5

Formulation Code	Average weight (mg)	Thickness (mm)	Hardness (N)	Friability %	DT(mins)
F1	119	3.34	70	0.10	2 min 09 sec
F2	120	3.35	62	0.10	2 min 52 sec
F3	119	3.34	62	0.11	2 min 55 sec
F4	120	3.35	70	0.10	4 min 03 sec
F5	120	3.35	68	0.15	3 min 20 sec
RLD	120	3.39	65	0.19	3 min 15sec

Table 5: Dissolution profile of formulations compared with innovator

Formulation Code	F1	F2	F3	F4	F5	RLD
Time in Minutes	**% Cumulative Drug Release**					
0	0	0	0	0	0	0
5	51	53	59	63	66	69
10	72	76	79	80	84	86
15	83	79	85	79	90	91
30	87	90	79	86	91	92
45	91	90	88	90	93	95

Reference:

1. Patel, H.P (2010). Formulation development & optimization of multiple unit particles system (mups) containing Ramipril and Hydrochlorothiazide. International Journal of Pharmaceutical Sciences 2010; 2(1):448-456.
2. Schwartz, B.J. (2000). Pharmaceutical Dosage Forms: Tablets. 75-130. Marcel Dekker, NewYork .
3. Collier, J.W., Shah, R.B. Bryant, A.R. Habib, M.J. Khan, M.A and Faustino, P.J. (2011). Development and application of a validated HPLC method for the analysis of dissolution samples of levothyroxine sodium drug products. J. Pharm. Biomed. Anal. 54, 433–438.
4. Collier, J.W., Shah, R.B. Gupta, A. Sayeed, V. Habib, M.J and Khan, M.A.(2010). Influence of formulation and processing factors on stability of levothyroxine sodium pentahydrate. AAPS PharmSciTech 2010, 11, 818–825
5. Patrick J Sinko. (2011). Martin's Physical Pharmacy, 6th Edn, woltersKluwer, 2011
6. Lachman, L., Leiberman, H and Kanig, J. (2018). 3rd Edn, "The Theory and practice of Industrial Pharmacy", 4thEdn, CBS Publishers and Distributors, Mumbai, 2018.

*****