CHAPTER-1
Introduction

Impurities in Drug Products

Drug synthesis involves multiple steps, in which an easily available chemical is ultimately converted in to the desirable product. It involves various other chemicals, such as reagents, catalysts and solvents. At each stage of synthesis, apart from the desired product, there can be formation of some undesired products and formation of some by-products which can be always present in the sample matrix (Watson, 2012) Therefore it is very much necessary to eliminate these contaminants before administration to the patient, to ensure safety of the patient.

It is very much necessary to ensure that, the drug administered to the patient, is pure and free from any impurities. It is because; these impurities don't have any therapeutic value they may cause adverse effect to the patient. Certain impurities based on their structural alert are reported to be mutagenic, carcinogenic and genotoxic in nature. Structurally associated impurities which are used as reactants or formed during synthesis as by products or side products or as degradants are called related substances. Catalysts, reagents and solvents used in the synthesis are not structurally associated with the drug substance (Berridge, 1995).

Related Substances

Related substances are impurities with structure similar to the drug substances. Based on their nature, these impurities are classified as process impurities and degradation impurities. Process impurities can be key raw materials, intermediates which are unconverted and still left in the final product. Some of the process impurities could be the by products or side products. By products are formed along with the desired product. Side products are formed because of the undesired path of the chemical reaction. Process impurities do not get formed or increased during stability or through out the life cycle of the product. Other process impurities could be the organic solvents, reagents, catalysts which were used in the process but not removed completely after purification. Organic

solvents are being used at various stages in the manufacturing including reaction, purification, crystallization followed by isolation. During purification step, process impurities are removed from the final product and their level is brought down to a minimum as far as possible (Grodowska and Parczewski, 2010).

Degradation impurities are the impurities, which are formed during the life cycle of the product. These impurities are formed as a result of degration of the active product. Degradation impurities are also formed during process itself. The level of formation of these degradation impurities are controlled by optimization of process parameters and the rate of increase of the impurities during lifecycle period are controlled by packing condition and maintaining the quality parameters under which the degradation could be observed minimum (Jang, 2016).

Non Related Substances

Non related substances are impurities which are not structurally related to the drug substances. These are inorganic reagents and catalysts used in the synthesis. They are controlled under elemental impurities and heavy metals. Inorganic salts are controlled by limit tests such as chloride content, sulphate content and residue on ignition. Elements which need to be controlled at low ppm level are quantified separately by using specific methods as defined by International conference on harmonization, ICH Q6A on test procedures and acceptance criteria for new drug substances and new drug products (ICH Q6A, 1999).

Organic Volatile Impurities

Organic reagents and solvents, which are volatile in nature, are used at various stages during drug synthesis. These solvents are used in the reaction process, purification and crystallization. These solvents are removed from the finish product at the final stage. It is achieved by effective drying process after filtration. Various drying techniques such as static bed drying, fluidized bed drying, spray drying, micro wave drying and rotary current drying were reported by Grodowska and Parczewski (2010). However, these drying processes have limitations with respect to their efficiency to remove these volatile impurities completely from the finish product. This may be due to the physical and

CHAPTER - 2

AIM AND OBJECTIVE

2.1 Aim:

From the literature survey conducted, it was found that there are few analytical methods reported for estimation of Cetearyl alcohol, Di-sodium EDTA and Dimethicone by using GC-FID.

A comprehensive, validated and simple analytical method for assay of Cetearyl alcohol, Di-sodium EDTA and Dimethicone and degradation products is therefore crucial. GC-FID with Flame ionization detector is a good selection as Flame ionization detector is available in most laboratories. Therefore, in proposed project a successful attempt has been made to develop simple, accurate and economic methods for analysis of Cetearyl alcohol, Di-sodium EDTA and Dimethicone and validated.

2.2. Objective:

The objectives of the present work are to development and validate a GC-FID method with Flame ionization detector for the assay of Cetearyl alcohol, Di-sodium EDTA and Dimethicone to be employed in routine and stability tests.

In the method development of Cetearyl alcohol, Di-sodium EDTA and Dimethicone. I have decided to carry out my project work by incorporating the Gas chromatography (GC-FID).

Finally the developed method will be validated according to ICH guidelines for its various parameters.

CHAPTER – 3

DRUG PROFILE

3.1 Drug profile of Cetearyl alcohol:

3.1.1Structure of Cetearyl Alcohol:

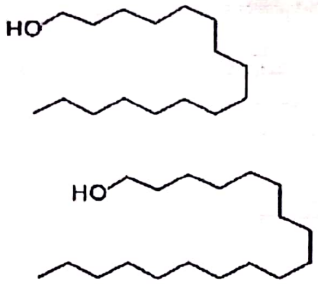

Figure No 11: Structure of Cetearyl alcohol

3.1.2Structure of Di sodium EDTA:

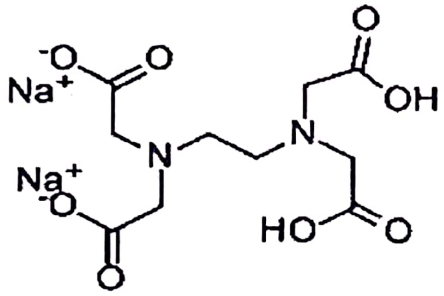

Figure No 12: Structure of Di sodium EDTA

3.1.3 Structure of Dimethicone:

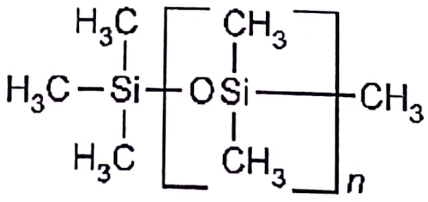

Figure No 13: Structure of Dimethicone

CHAPTER -4

PLAN OF WORK

In order to develop a simple, reliable and accurate method for the assay of Cetearyl alcohol, Di sodium EDTA and Dimethicone samples by GC-FID and validate the method for its repeatability and reproducibility.

The plan work includes:

- ✓ Procurement of raw materials.
- ✓ Establishment of system suitability parameters.
- ✓ Trials for the method development for Cetearyl alcohol, Di sodium EDTA and Dimethicone Setting the optimized method.
- ✓ Validation of optimized methods for Cetearyl alcohol, Di sodium EDTA and Dimethicone

Validation parameters like:

- ❖ System suitability and system precision.
- ❖ Specificity
- ❖ Linearity and range.

CHAPTER -5

MATERIALS AND EQUIPMENTS

5.1 CHEMICALS AND REAGENTS:

Table No 6: Chemicals and Reagents

S.NO	NAME OF REAGENT	MAKE	GRADE
1	Methanol	Rankem	HPLC Grade
2	Acetonitrile	Merck	HPLC Grade

5.2 STANDARDS AND SAMPLES:

Table No 7: Standards and Samples

S.NO	NAME OF THE DRUG	MANUFACTURER OR SUPPLIER
1	Cetearyl alcohol working standard	Cipla Laboratories pvt.Ltd
2	Di sodium EDTA	Cipla Laboratories pvt.Ltd
3	Dimethicone	Cipla Laboratories pvt.Ltd

5.3 INSTRUMENTS OR EQUIPMENTS DETAILS:

Table No 8: Instruments or equipment's

S.NO	INSTRUMENT NAME	MAKE AND MODEL
1	GC-FID	8890 GC System with 7693A
2	Software	N 2000
3	Model	Omega
4	Detector	Flame Ionization detector
5	Ultra sonicator	Unichrome
6	pH meter	GT Sonic
7	Electronic balance	Ohaus
8	GC Column	Zorbax Sp 250 x 300mm, 10µ
9	Centrifuge	Remi
10	Refrigerator	Whirlpool

CHAPTER -6

EXPERIMENTAL DETAILS

6.1 Preparation of Standard Solution:

1µg/ml of Cetearyl alcohol, 10µg/ml of EDTA and 100µg/ml of Dimethicone are prepared by diluting with mobile phase. This solution is used for recording chromatogram.

6.2 Preparation of sample Solution:

Weigh 1g of Vaseline and Himalaya Body lotion into different 100ml volumetric flasks and make up to the mark with diluents

6.3 Analytical method validation:

6.4.1 Steps involved in method validation:

The scope of the method and its validation criteria should be defined early in the process.

6.4.2 Possible parameters for method validation:

The following parameters were considered for the analytical method validation for assay of Cetearyl alcohol, Disodium EDTA and Dimethicone in health care products.

1. System Suitability
2. Specificity / Selectivity,
3. Linearity and range

6.4.2.1 System suitability:

The standard and check standard solutions were prepared as per test method and injected into GC-FID system. The system suitability parameters were evaluated as per the test method and found to be within the limits.

6.4.2.2 Specificity:

Specificity is the ability to asses unequivocally the analytic in the presence of components which may be expected to be present. Typically these include impurities, degrades, matrix, etc.

6.4.2.3 Linearity:

CHAPTER -7

RESULTS AND DISCUSSIONS

7.1 Spectrum:

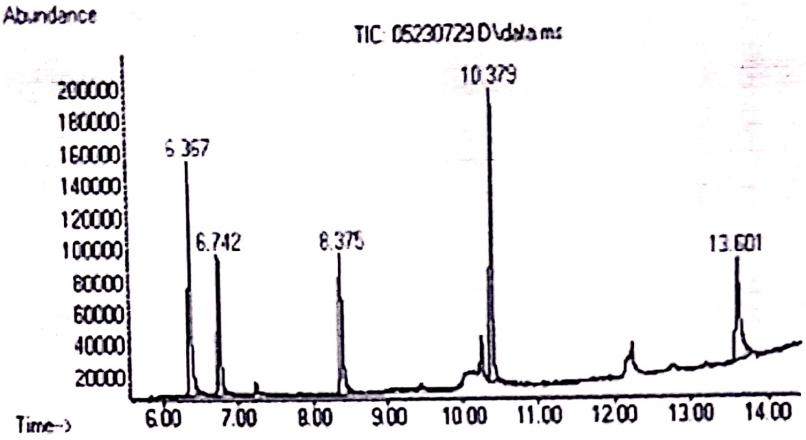

Figure No 14: spectrum

7.2 ANALYTICAL METHOD VALIDATION OF CETEARYL ALCOHOL, EDTA AND DIMETHICONE

7.2.1Specificity:

BLANK

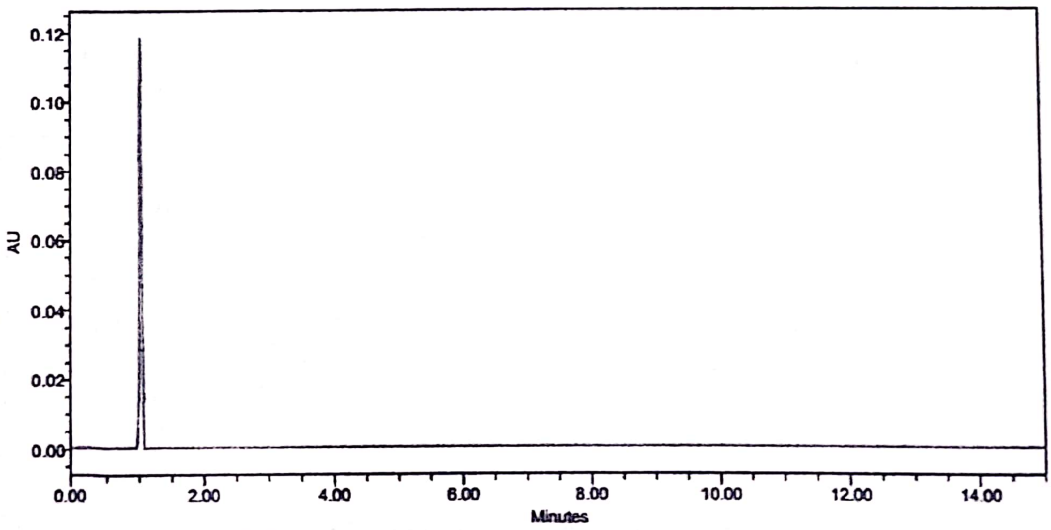

Figure No 15: - Typical Chromatogram of Blank

S.No.	Name	Rt (min)	Peak Area
1	Blank	-	-

CHAPTER –8: SUMMARY AND CONCLUSION

An attempt has been made to develop a validated stability indicating GC-FID method for the estimation of Cetearyl alcohol, Disodium EDTA and Dimethicone.

Chapter– 1 Gives the general information on GC-FID and method development.

Chapter-2 Discusses about drug profiles and official status of selected drugs i.e., Cetearyl alcohol, Disodium EDTA and Dimethicone.

Chapter - 3 Explains in detail the previous literature available for drugs used for developed research work.

Chapter - 4 Gives in detail about the aim, objective and plan of the proposed work by using selected drugs.

Chapter - 5 Include Stability Indicating GC-FID Method Development and Validation for Estimation of Cetearyl alcohol, Disodium EDTA and Dimethicone in Bulk and their Pharmaceutical dosage form. Using GC system, with Omega QC+ and the software is N 2000 and the mobile phases are Hydrogen, Helium, Nitrogen and Zero air and detected by Flame Ionization detector detector. The peak of Disodium EDTA, Cetearyl alcohol and Dimethicone was eluted at retention times of 2.352, 5.930 and 7.384 min.

Chapter- 6 In this proposed GC method for the selected drugs showed good linearity. Results for the recoveries of selected drug was found to be within limits (98 – 102 %). These indicate that the proposed method was accurate for the analysis.

CHAPTER -9

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