Simultaneous determination of multi-components drugs in liquid and semi-solid dosage forms by High- Performance Liquid Chromatography

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To my parents

my wife

my brothers, sisters

and all my friends

with love and respect

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The key of great education lies in the developmental stages of its evolvement, I believe that the difficulties, triumphs and anxieties encountered during our progression through these various stages help us not only in the enhancement of our knowledge and in the satiating of our curiosity, but it also plays a fundamental role in the strengthening of our character and in the resilience of our stamina. All of the diligent work involved in obtaining my Master of science in applied and industrial technology was indeed worthwhile and fulfilling; not to mention trying at other times , however throughout all of this, there were those who I could count on for their wisdom, assistance and support which served as an essential driving tool in my encouragement to achieve this degree, therefore, I would like to take this opportunity to extend my sincere gratitude to all of them.

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LIST OF ABBREVIATIONS

Abbreviations

P	**Pseudoephedrine hydrochloride**
CP	**Codeine phosphate**
T	**Triprolidine hydrochloride**
B	**Betamethasone**
C	**Clotrimazole**
B.N.	**Batch Number**
A.I.	**Active Ingredient**
SD	**Standard deviation**
RSD	**Relative Standard deviation**
K'	**Capacity factor**
AU	**Absorbance Unit**
HPLC	**High-Performance Liquid Chromatography**
GC	**Gas Chromatography**
GLC	**Gas Liquid Chromatography**
TLC	**Thin Layer Chromatography**
UV	**Ultraviolet**

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ABSTRACT

HPLC methods have been developed for the simultaneous determination of the combinations of Pseudoephedrine HCl, Codeine phosphate and Triprolidine HCl in liquid dosage forms and the combinations of Betamethasone and Clotrimazole in semi-liquid dosage forms with the same chromatographic conditions except the percentage of the mobile phase which is methanol-acetate buffer-acetonitrile (85:5(100mg/l):10) for the first combinations and (33:27(25mg/l):40) for the second combinations. The reversed-phase method utilizes UV detection at 254nm, a C18 column, the flow rate is 1.5ml/minuets and requires 5 minuets per analysis for the first combinations and 8 minuets for the last combinations.

The methods have been validated for use with syrup in the linearity ranges of (0.06-21.0mg/ml) with a correlation coefficient of 0.9996 for **P**, (0.02-1.0mg/ml) with a correlation coefficient of 0.9997 for **CP** and (0.002-1.0mg/ml) with a correlation coefficient of 0.9993 for **T** and with cream in the linearity ranges of **B** (0.006-0.2)mg/ml with a correlation coefficient of 0.9996 and of **C** (0.06-25.0)mg/ml with a correlation coefficient of 1.0. A detection limit of (0.008), (0.001) and (0.0006)mg/ml for **P**, **CP** and **T**, respectively, and a detection limit of (0.00008) and (0.002)mg/ml for **B** and **C**, respectively. The recovery data for each compounds were determined (99.77+/-0.25%), (99.38+/-0.74) and (98.58+/-1.28) for **P**, **CP** and **T**, respectively, and (99.54+/-1.99) and 98.75+/-1.51%) for **B** and **C**, respectively. The first method was applied to commercial products and the results obtained were (102.91+/-0.35%), (97.25+/-0.65%) and (96.33+/-2.09%) for **P**, **CP** and **T**, respectively, and the second method was applied to commercial products and the results obtained were (92.31+/-1.06%) and (99.58+/-1.52%) for **B** and **C**, respectively. The methods have been shown to be simple, accurate, sensitive, fast and having a wide linear ranges and low detection limits which are better than any other old methods were used. The above mentioned methods may be used either in-

FORWARD

The analysis of liquid dosage forms of pharmaceutical preparations that contain more than one active constituent, along with various dyes, flavors, preservatives and sweeteners is very difficult. The use of high-performance liquid chromatography (HPLC) has become a powerful technique in the successful analysis of these dosage forms. The HPLC techniques employed include normal-phase, reversed-phase and ion-paired chromatography .

Many Drugs contain a number of active ingredients to cater for the therapeutic needs. The action properties, and the structures of these ingredients have been studied in details in various references[2-12,30-36]. High Performance Liquid Chromatography (HPLC) is an important method for the analysis of drugs because it is accurate and simple, also using this method is useful for identification of the drug components, especially the active and the important inactive components as the preservatives. HPLC is important in the analysis of small amounts components as the chemical degrades of the stability studies or for small doses drugs .

The purpose of this study is to present a new and simple quantitative and qualitative test methods for Pseudoephedrine HCl, Codeine phosphate, and Triprolidine HCl in liquid dosage form, and Betamethason and Clotrimazole in cream dosage forms.

The objective of these test methods is to generate reliable and accurate data for acceptance of raw materials, release of the drug substances and products, in-process testing for quality assurance, and establishment of the expiration dating period.

This study is divided into two parts A and B:

Part A:

Pharmaceutical combination of ***Pseudoephedrine HCl, Codeine phosphate, and Triprolidine HCl***, are adrenergic decongestant or sympathomimetic, narcotic analgesic, and antihistaminic, respectively . The local product which contains this combination is ***Tussibal compound syrup***, manufactured by Jerusalem Pharmaceuticals Co. Ltd., Al-Bireh. The label claim for Tussibal compound syrup is as follows :

Each 5 ml of Tussibal compound syrup contains :

Pseudoephedrine HCl	30mg
Codeine phosphate	10mg
Triprolidine HCl	1.25mg

The Therapeutic Activity for Tussibal compound syrup is for the relief of cough due to colds or influenza .

Part B:

Pharmaceutical combination of ***Clotrimazole and Betamethasone*** , are antifungal and anti-inflammatory action . The local product which contains this composition is ***Beta-canazole cream***, manufactured by Jerusalem Pharmaceuticals Co. Ltd., Al-Bireh. The label claim for Beta-canazole cream is as follows :

Each tube contains :	
Clotrimazole	1%w/w
Betamethasone	0.1%w/w

The therapeutic activity for Beta-Canazole cream is for the treatment of the following dermal infections :tinea pedis, tinea cruris, and tinea corporis due to Trichophyton rubrum, Trichophyton mentagrophytes, Epidermophyton floccosum, and microsporum canis .

The Goal of This Research Project

The combinations (Pseudoephedrine HCl, Codeine phosphate, Triprolidine HCl) and (Betamethasone, and Clotrimazole) have no official simultaneous assay. The traditional separation methods for the determination of active ingredient in the above mentioned combinations are time consuming. This long time during manufacturing may expose the batch to contamination. In addition, the results are not accurate.

Therefore a new method is needed to determine the active ingredients for the above mentioned pharmaceutical combinations which is applicable for either in-process testing or final testing. The goal of this work is to establish HPLC methods that have excellent analytical parameters.