

Determination of Theophylline Stability in New Cream Formulation

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Abstract: To determine the stability of theophylline in theophylline cream, its concentrations in this new formula was determined after storage at room temperature. Addition of preservatives in theophylline cream makes the formula contains a stable concentration of theophylline for a long periods of storage time with no changes in physical properties. While, theophylline in cream that have no preservatives showed less stability at the end of storage time.

Key words: Cream, physical property, preservative and theophylline

INTRODUCTION

Theophylline, 1,3-dimethylxanthine, is widely described for the treatment of asthma and chronic obstructive pulmonary disease (COPD) (Barnes, 2003). For pharmaceutical usage, theophylline can be manufactured to produce many forms including tablets, capsules and syrups. Similar to other medicines, theophylline drugs affected by temperature either in human body or during storage time. In human body, decreasing of pharmacokinetics and elimination of theophylline is associated with increasing of environmental temperature (Schlaeffer *et al.*, 1984; Matsuama *et al.*, 1984). Jonkman *et al.* (1981) found that theophylline can stable in serum for 15 days, in plasma for 11 days, and 18 days in saliva after storage at room temperature (25°C). Moreover, stability study of theophylline tablets that stored at 40 °C revealed that there was no significant changes in the drug compositions, hardness and friability (Deshmukh *et al.*, 2009). However, theophylline has the ability to retain 90% of its amount in 30 years old tablet beyond expiration date (Regenthal *et al.*, 2002).

The aim of this study is to prepare a new formula of theophylline consists of cream drug with determination of its stability at room temperature.

MATERIALS AND METHODS

This study was carried out in the laboratories of college of pharmacy- university of Karbala (Iraq) in March 2009.

Chemicals: Theophylline anhydrous was purchased from HiMedia, Mumbai-India. Methylparaban (MP), propylparben (PP) and cream were supplied from SDI, Samara-Iraq.

Drug preparation: Theophylline was stirred with cream base by glass rod on hot plate until homogenization. Prepared cream was divided into two groups. First group

consists of theophylline cream (50 mg of theophylline per gram of cream) and second consists of above cream with addition of preservative agents (0.001 mg of MP and PP per each gram of theophylline cream). Fresh drugs were distributed in plastic cups with 5 gm for each. Cups were incubated at 25 °C for various periods of time.

Determination of drug concentrations: Theophylline cream was dissolved in Na₂CO₃ (0.5 N) and mixed for 10 min in separating funnel. After standing for 5 min, two layers were separated and filtered by Whatman filter paper. From filtered solution, 0.1 ml was diluted to obtain 40 mg/L. The diluted was analyzed by UV-Visible 1800 spectrophotometer (Shimadzu, Kyoto-Japan) at 284 nm (De Fabrizio, 2006) for determining theophylline concentration.

Physical characters, including texture, color, odor and hardness of prepared drug were noted during the periods of experiment.

Statistical analysis: Result data were statically analyzed by using two-way variance of analysis (ANOVA) with less significant difference (L.S.D) at P<0.05.

RESULTS AND DISCUSSION

Measurement of theophylline concentrations in cream formula by spectrophotometer assay was utilized as indicator for theophylline stability. Although constant concentrations of theophylline in cream with preservative persisted for 49 days, decline of these concentrations either in cream without preservative or in cream with preservatives began to be cleared after 56 days of storage at room temperature (Fig. 1, 2).

Additionally, physical characters of cream containing preservatives showed no changes during storage time. While, cream without preservatives exhibited a few signs of dryness and color changing.

Many drugs stored under reasonable conditions retain 90% of their potency for at least 5 years after the expiration date on the label, and sometimes much longer.

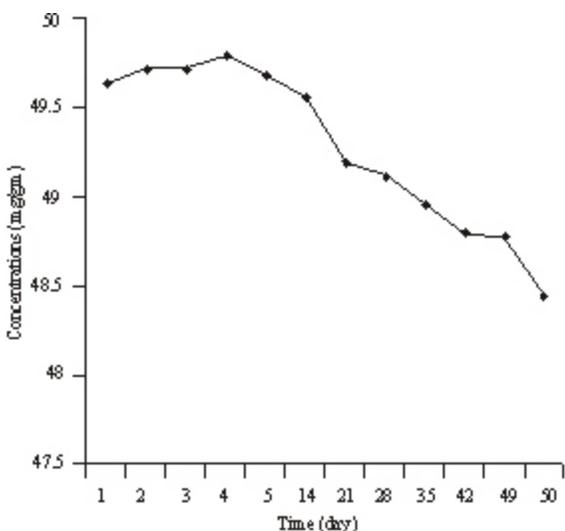


Fig. 1: Concentrations of theophylline in cream without preservatives after several periods of time

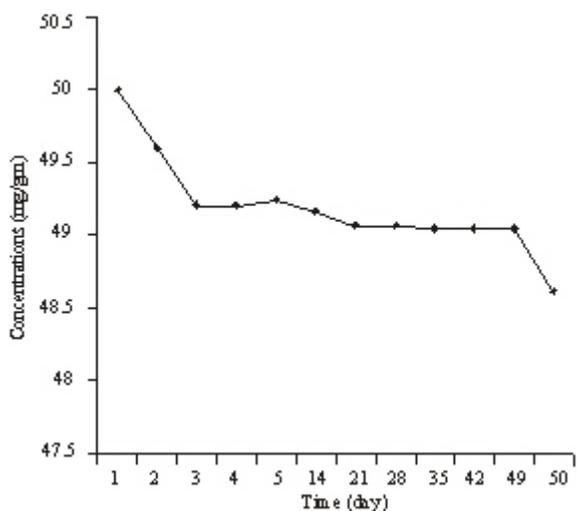


Fig. 2: Concentrations of theophylline in cream with preservatives after several periods of time

Theophylline found to be retained 90% of its potency for about 30 years (Abamowicz, 2002). Many factors may influence on theophylline stability in pharmaceutical drugs. Temperature is the most important factor that effects on stability, action, release and elimination of theophylline from their drugs. The release rate of theophylline from hydrogels form was increased by increasing temperature, due to the effect of temperature on mobility of molecules and the higher temperature elevated molecules mobility through diffusion process (Liu *et al.*, 2005). From other hand, Sipmann *et al.* (2008) found that addition of small amounts of additive under ambient conditions may increase stability of theophylline in pellets.

Preparation of theophylline cream in present our study may add a new formula to ordinary list of

pharmaceutical dosage forms of theophylline. In previous study, theophylline cream (50 mg/gm) showed high efficiency to cure dermatophytoses disease (AL-Janabi, 2004). For evaluation of this formula, stability of theophylline cream was tested at room temperature. It showed a high degree of stability after 49 days with no changes in physical properties of cream when preservatives were added.

Growth of microorganisms in cream can cause physical separation of its compositions. Thus, adequate concentrations of preservatives must be added in produced drug to prevent degradation of these compositions by microorganisms.

The main effects of temperature on cream characters is through elevating of evaporation rate (Frisbee *et al.*, 2004) that can yield dryness cream. Homogenization of cream is another factor could be associated with temperature. Good homogenization process may decrease the effects of heat on cream stability (Webb, 1931).

In conclusion Theophylline cream showed successful formula with high stability at room temperature for a long period of times.

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