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Research Article

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Coating Efficiency in Preventing Photolytic Degradation of Two Randomly Selected Brands of Metoprolol Tartrate

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ABSTRACT

This research work was carried out to determine whether the film coating is effective to prevent the photolytic degradation of Metoprolol tartrate which is known to have photosensitivity. For this purpose, two randomly selected brands of two different pharmaceutical companies were chosen *i.e.* Brand A and Brand B. These two brands were exposed to different lighting conditions (normal light, direct sunlight as well as two incandescent lights i.e. 25 watt bulb, 40 watt bulb). Potency tests were performed using UV spectroscopy which showed gradual decline in potency of the tablets under aforesaid lighting conditions and the potency degradations were found 11.48%, 12.92%, 22.62%, 16.87% for Brand A and 14.74%, 14.24%, 10.88%, 18.10% for Brand B under 25 watt bulb, 40 watt bulb, direct sunlight and normal room light respectively. So this study reveals that the both brands containing metoprolol tartrate showed significant light sensitivity even though they are coated and protective opaque packaging is highly recommended for their protection.

Keywords: Metoprolol Tartrate, Potency, Light, Incandescent, Photolytic Degradation, Photosensitivity, opaque packaging.

INTRODUCTION

For the treatment of various heart diseases, beta blockers or beta adrenergic blockers are a significant class of medication. They are used in arrhythmias, hypertension, angina pectoris etc. The catecholamines (epinephrine and nor-epinephrine) are released from the nerve endings of sympathetic nervous system which enables our body to mitigate the effect of anxiety and stress. In fact, catecholamines stimulate the specific cell surface receptors known as adrenoceptor. Beta adrenergic receptors are mainly found in heart, lung and blood vessels. These receptors can be activated upon the binding of catecholamines with them resulting various physiological responses. These premium responses included heart muscle contraction, increase in HR and BP, but relaxation in bronchial muscles. When beta blockers are administered, they inhibit the catecholamines to bind the beta adrenergic receptors and lower the blood pressure and heart muscle contraction. [1-3]

There are mainly three types of beta adrenergic receptors. Beta 1 receptors are mainly found in heart and kidney whereas beta 2 receptors are found in lung, GIT and liver. Beta 3 receptors are commonly found in fat cells. [4-5] Beta blockers which bind with all the beta

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receptors are called non-selective beta blockers. On the other hand, those drugs which block only beta 1 receptors are termed as cardio selective beta 1 blocker. A major drawback of non selective beta blockers is that they block beta 2 receptors along with beta 1. This unexpected blocking can result in bronchial constriction producing asthma, emphysema etc. However, cardio selective beta blockers give a clinical advantage in affecting the heart, which predominantly has beta1 receptors. The impact of broncho-constriction is less with beta 1 selective blockers, as the bronchial muscle has more beta 2 receptors, however the possibility of broncho-constriction cannot be totally ignored, as they are not totally selective. [6-7]

Metoprolol tartrate is selective beta 1 adrenergic blockers. It predominantly blocks beta 1 adrenergic receptors and lowers blood pressure, and cardiac contraction. [8-9]

Photolytic degradation refers to the chemical decomposition process by which light-sensitive molecules are chemically modified by room light, extreme light, direct sunlight or other electromagnetic radiation. [10] Photo degraded products may result from the exposure of drug molecule to the visible or UV light. The kinetics of photo degradation in related to the intensity of incident light and quantity of absorbed light by the drug molecule. Photolytic degradation is carried out by exposing the drug product to a combination of visible and UV light. The wavelength from 300 nm to 800 nm is usually the accepted range for photolysis. [11]

In the local market of Bangladesh, several manufacturers produce and market Metoprolol tartrate and many of those are with normal transparent blister packaging. However, some of those are coated and there are some reports regarding photosensitivity of Metoprolol tartrate [12-13] therefore the objective of this research project was to determine whether the film coating is sufficient enough to prevent the photolytic potency reduction of Metoprolol Tartrate. In this study, potency change due to light sensitivity of metoprolol tartrate was determined in various lighting conditions (normal light, direct sunlight and 2 incandescent lights i.e. 25 watt bulb, 40 watt bulb). For this purpose, two brands were randomly chosen *i.e.* Brand A and Brand B with coating which are marketed in transparent blister packaging system.

MATERIALS & METHOD

For the purpose of experimentation to observe the photolytic degradation of Metoprolol Tartrate as well as to assess the film-coating efficiency, sufficient number of tablets of both brands were collected from a local drug store in Dhaka, Bangladesh. Among them some tablets from both brands were kept away from light protection for control tests and the remaining tablets were subjected to various lighting conditions over certain periods of time with a view to conducting experiments to determine their potency.

Instruments Used: Instruments used in this research were Shimadzu UV 1800, Japan; Bibby Scientific W 4000, UK; Electronic balance Shimadzy AY 220, Japan.

Preparation of Standard Curve: 0.1N Sulfuric acid was prepared from the 98% (w/v) Sulfuric acid stock solution provided by the university laboratory. Nine concentrations of metoprolol tartrate was prepared using 0.1N H_2SO_4 to obtain 0.001-0.009 mg/ml. All the absorbances were measured at the λ_{max} (221.5nm) and plotted against the above concentrations (Fig. 1). This standard curve was finally used to calculate the potencies of both brands of metoprolol tartrate against the absorbances found.

To determine the photo stability of the drug within their film coating, tablets were differently exposed to various lighting conditions such as normal light, 25 watt bulb, 40 watt bulb, direct sunlight. Under different lighting conditions tablets were sampled periodically for determining the potency.

Normal Room Light Exposure: Under normal lighting condition 60 tablets were kept for three months and 10 tablets from each brand were tested at 0, 15, 30, 45, 60 and 90 days. This experiment was carried out 3 times to ensure reproducibility.

Incandescent Lighting Condition Exposures (25W and 40W bulbs): Under Incandescent bulb light conditions 60 tablets were exposed from which 5 sets (total 15 tablets) were tested at 0, 2, 4 and 6 hours. This experiment was carried out 5 times to ensure reproducibility.

Direct Sunlight Exposure: Similar procedure was followed for the tablets exposed under the direct sunlight as for the incandescent lighting conditions.

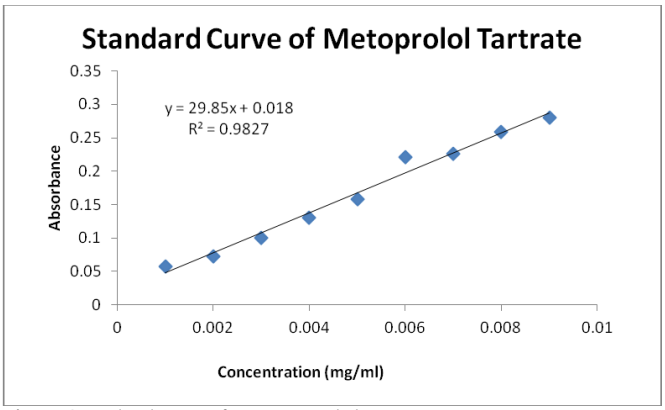

Fig. 1: Standard curve for metoprolol tartrate

RESULTS AND DISCUSSION

In this study, all the experiments under different lighting conditions showed gradual degradation. In all of these tests only the Controls (unexposed to light) were with consistent potency whereas the two brands chosen showed marked degradation although they had coating. However, our study tried to find out whether this coating was enough to prevent photolytic degradation in normal room light (Fig. 2 & 3) as well as in three extreme conditions (Fig. 4, 5, 6, 7, 8 & 9). In the extreme conditions (25 W bulb, 40W bulb as well as

Direct Sunlight exposures), an extreme level of photosensitivity was detected for both brands. Among these experiments, the direct sunlight had the most serious effect on the potency for brand A, but interestingly it had the least effect on Brand B (Fig. 8 & 9), However, in the two other extreme conditions (the 40 W bulb and 25 W bulb respectively), both brands showed almost similar kind of marked degradation (Fig. 4, 5, 6 & 7).

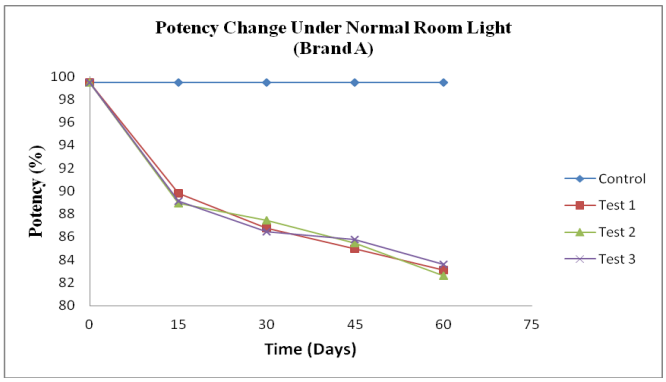

Fig. 2: Normal Light Exposure Results (Brand A)

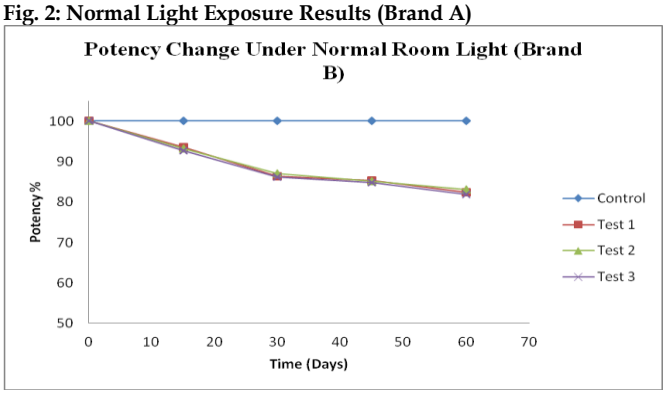

Fig. 3: Normal Light Exposure results (Brand B)

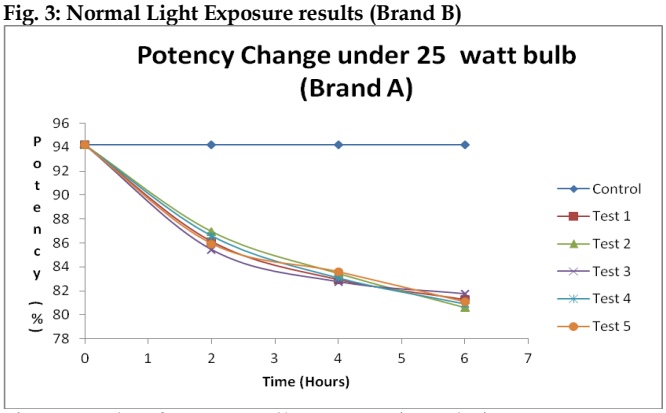

Fig. 4: Results of 25 Watt Bulb Exposure (Brand A)

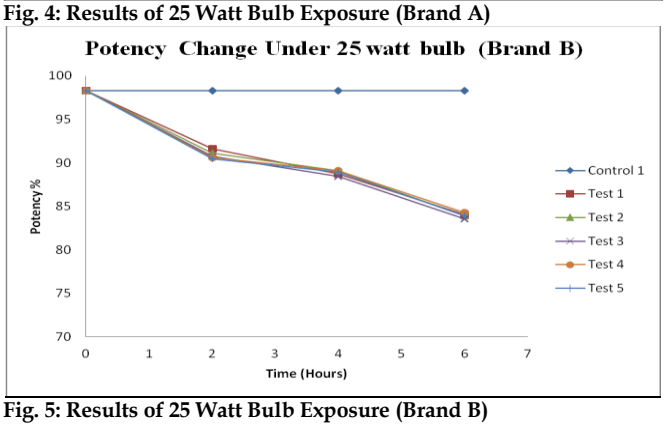

Fig. 5: Results of 25 Watt Bulb Exposure (Brand B)

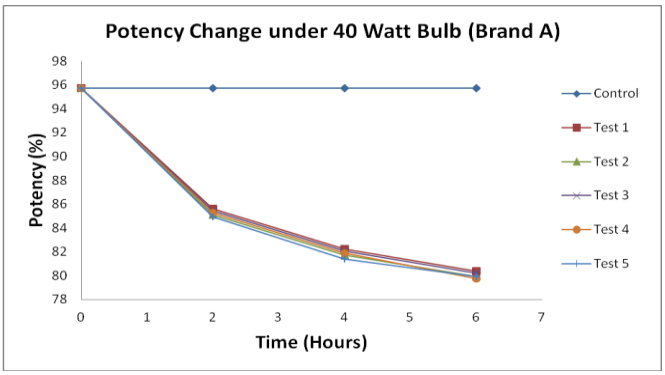

Fig. 6: Results of 40 Watt Bulb Exposure (Brand A)

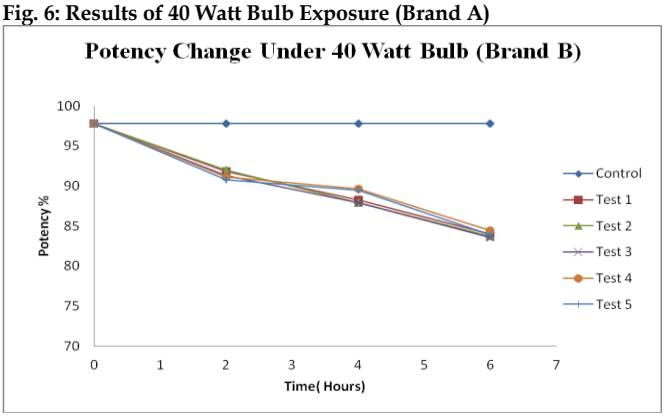

Fig. 7: Results of 40 Watt Bulb Exposure (Brand B)

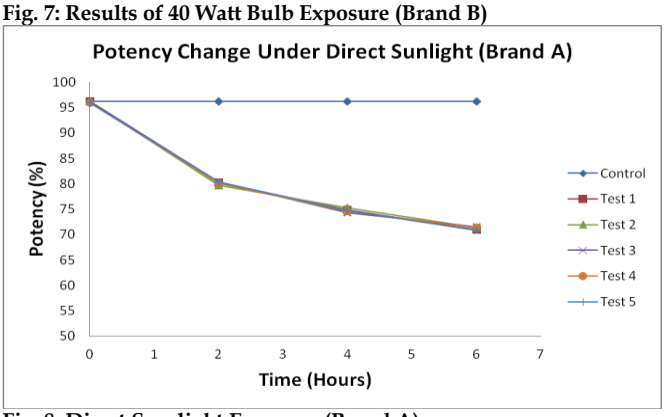

Fig. 8: Direct Sun-light Exposure (Brand A)

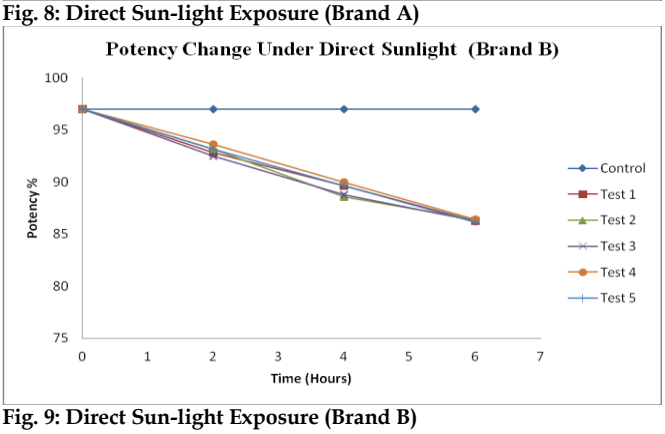

Fig. 9: Direct Sun-light Exposure (Brand B)

However, the temperatures recorded during these experiments were very close to each other although the 25W bulb had the lowest. The temperature at the beginning of both 25W bulb as well as 40W bulb was the same *i.e.* 25°C, but after six hours the temperatures were 34°C and 35°C respectively. But we see a clear degradation pattern difference between them (Fig. 4, 5, 6 & 7) *i.e.* the 40W light showed more degradation. On the other hand, under the direct sunlight which was

started during the summer season in Dhaka, the temperature started with 28°C at 9 o'clock in the morning and after six hours it was recorded 35°C which we can consider same as those for the bulb lights. However, it showed higher level of degradation (Fig. 8 and 9) than the other two extreme types, probably because of a higher starting temperature and/or more intense sunlight with the full spectrum. [14]. It was really surprising to have different scenario of degradation between these two brands (Fig. 8 & 9) although they both were exposed on the same day and kept side by side under the same lighting condition. One probable reason of the less degradation brand B may be for the coating materials used in it are more stable to sunlight exposure. The similar result was also found in the normal room-light exposures (Fig. 2 & 3). Here it was seen that Brand A had sharp fall in potency (almost 12% potency drop) during the first 15 days whereas brand B degraded little slowly (close to 8% potency fall) during this time although at the end of 60 days both lost their potencies almost by 20%. Metoprolol is already known to have photosensitivity [12-13] and all the results in this study again proved it even in the presence of coating.

Lastly, it is necessary to add that in the normal room-light conditions these brands faced various temperatures (20°C to even 30°C). Nevertheless, the Pharmaceutical companies also run some elevated temperature studies according to USFDA [15] guidelines which are much higher than our experiment temperatures and these formulations also went through those tests we believe and they passed. Therefore, it can be concluded that, the degradations were principally due to light and a better protection such as a much thicker coating or light-protected packaging should be chosen for such drugs.

Photosensitivity is a common reason for the degradation of pharmaceutical products. [16] Although, the photodegradation of metoprolol tartrate is rare but not unusual. As a widely prescribed medicine [17-18] it should be more carefully packaged into a light protective opaque packaging to prevent the formation of any light-degraded by-product of this anti-hypertensive drug.

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