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# Light transmission properties of pharmaceutical liquid bottles and evaluation of their photoprotective efficacy

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**Abstract**: The light sensitive pharmaceutical dosage forms are well protected from light by packing in light protective bottles especially the colored glass and plastic bottles. In the present study the transmission characteristics of transparent glass bottle, amber glass bottle, polyvinyl chloride amber plastic bottle (PVC) and low density polyethylene semi-opaque plastic bottles (LDPE) (empty and drug filled) have been evaluated and the data compared for compliance with Pharmacopoeial limits of percentage transmission. The variations in thickness affect the amount of light transmitted through the bottles. For an average thickness, the transmission of bottles was not uniform indicated the effect of manufacturing variables on the transmission of light. The drug filled bottles showed an increase in light transmission probably as a result of interaction between drug and bottle components. The leaching of any coloring agents from glass bottles or the pigments from plastic bottles into the solution during storage appeared to increase the transmission of light which could be detrimental to photosensitive drugs in a formulation. The light protective efficacy of bottles was in the order: Semi-opaque plastic (LDPE) > amber plastic (PVC) > amber glass. The photoprotection of aqueous solution of riboflavin as a model compound in these bottles has been studied and its shelf-lives and stability ratio were determined.

**Keywords**: Light transmission, pharmaceutical bottles, photoprotection, riboflavin, stability.

## INTRODUCTION

Packaging is stated as the technology and art of preparing a product for convenient storage, utilization, transportation, sales and marketing. Pharmaceutical primary and secondary packaging materials are the expression of the brand identity of the pharmaceutical product and are essential for its fundamental qualities (Sabah *et al*., 2014). Light causes deterioration of many pharmaceutical products due to its transmission from the primary bottles. The effect of light increases and is much more harmful as the wavelength of light decreases. Light sensitive products must be packaged in amber glass and plastic bottles because these are manufactured to absorb light in the UV region to protect the pharmaceutical products (Templeton *et al*., 2005; Tonnesen, 2008) The transmission characteristics of different glass and plastic bottles assist in photoprotection of drugs in the UV and visible region have been reported (Templeton *et al*., 2005; DeGrazio, 2006; Allain and Wang, 2007; Andrady and Mike, 2009).

It has been observed that the use of substandard and low grade packaging materials including glass and plastic bottles may lead to stability problems in pharmaceutical products (Sabah *et al*., 2014). The measurement of light transmission characteristics of glass and plastic bottles is an important consideration in the evaluation of packaging material to protect pharmaceutical products from deterioration (Loftsson, 2014). The British Pharmacopoeia (BP) (2016) and the United States Pharmacopeia (USP) (2016) have provided limits of light transmission in the 290-450 nm region for glass and plastic bottle as shown in table 1. The transmission of light from the bottles depends also on the wall thickness of the bottles, so the Russian GOST standard prescribes a limit value dependent only on wall thickness. No distinction is made between types of bottle or filling volumes (Roessler, 2011). The transmission characteristics of different glass and plastic bottles in the UV and visible region may enable their selection for compliance with the specifications of different Pharmacopoeias to protect photosensitive drugs from degradation (Coltro and Borrghetti, 2007; Roessler, 2011).

The pharmaceutical grade colored glass is obtained by the addition of small amounts of metal oxides, the yellow green glass contains chromium oxide and the medium green contains iron oxide. The light transmission can be influenced by altering the chemical composition of glass bottle, so not all amber bottles provide sufficient protection against UV light. The extent to which UV light can cause a photochemical reaction is dependent on its penetration to the system. For pharmaceutical products it would depend on the degree of transparency of the packaging material. The transmission curve of a bottle can only be described in terms of its defined composition and thickness (Tonnesen, 2004). The colorless and blue glass transmits high level of UV wavelengths, the yellow-green transmits no UV and the amber transmits very little UV light. The amber and yellow-green glasses are more

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effective in protecting the contents of bottle from the effect of sun light by screening out harmful UV rays (Piechocki, 2007). The amber color of glass is out shined by the addition of iron and manganese oxides whose cations are known to catalyze oxidative reactions and are extracted from the glass (Jaime *et al*., 2018). Several studies have shown that the degradation rates of different drugs like amitryptylin (Chen *et al*., 2017) and L-ascorbic acid were enhanced in amber glass bottles of different composition due to UV absorption (Robertson, 2010). The photochemistry of the organic compound has also been studied for a long time and advance treatment of the subject is available (Ravelli, 2015). The degradation of photosensitive drugs such as cyanocobalamin (Arsalan *et al*., 2020) and riboflavin (Ahmad *et al*., 2015) is greatly enhanced by exposure to visible light and that of metronidazole (Farzadkia *et al*., 2015), quinolones like norfloxacin (Ahmad *et al*., 2016) ofloxacin and levofloxacin (Frąckowiak *et al*., 2016) and ibuprofen, cetirizine, and naproxen (Mohamed *et al*., 2018), by UV light.

Any light that is not absorbed by a glass or reflected at its surface will be transmitted through the glass. It is often very important to know exactly how much light will pass through a glass at specified wavelengths. Often, glasses are discussed in terms of their transmittance or transmission. The same information is provided by both of these terms but transmission is reported with ranges from 0% to 100% and transmittance from 0 to 1 (Galbraith, 2015). Radiation energy from artificial sources either UV or visible light significantly affects the stability of photosensitive products, since it accelerates photochemical degradation reactions that have a product deterioration effect. In addition the plastic bottles are known to contain polymers that undergo oxidative degradation when exposed to light, thereby causing discoloration and weakening of the polymer (Espinoza-Atencia *et al*., 1993). This would affect the light transmission characteristics of the plastic and hence the stability of the pharmaceutical product. UV rays carry more energy than visible light and cause greater damage. For this reason, organic compounds are used as light stabilizers in a wide variety of plastic resins to prevent photodegradation caused by sunlight and artificial UV light (Silverstein and Bassler, 1987). Most UV light absorbers are derived from benzophenone or benzotriazole and act in the initial phase of the degradation process as they absorb UV radiation and prevent the formation of free radicals. Polyolefins alone [polypropylene (PP), high density polyethylene (HDPE) and low density polyethylene (LDPE)] are responsible for more than 70% of the light protective materials marketed in the world (Zweifel, 2001).

Since light has a strong catalyzing effect on the oxidation of pharmaceutical products, the amount of residual oxygen in the headspace of the package is sufficient to catalyze photo oxidation reactions that affect certain components of the pharmaceutical products. The packages must have low oxygen permeability and packaging materials should contain some additives with high light barrier properties to avoid photodegradation (Coltro and Borghetti, 2007).

The main object of this study is to evaluate the light transmission characteristics of amber glass bottles, amber plastic bottles (PVC) and semi-opaque plastic (LDPE) bottles used in pharmaceutical industries to show their compliance with the pharmacopoeial specifications for the packaging of photosensitive pharmaceutical products and any variations due to drug bottle interaction on packaging and storage of the products. It is also intended to study the photostability of a highly photosensitive riboflavin (vitamin $B_2$), as a model drug (Ahmad *et al*., 2015a) in these bottles and to compare their photoprotection efficacy in terms of the shelf-life of riboflavin.

## MATERIALS AND METHODS

Riboflavin (RF), lumichrome (LC), lumiflavin (LF) were purchased from Sigma Aldrich, St. Louis, MD, USA. All solvents and reagents were of analytical grade or of purest form available from Merck & Co. Whitehouse Station, NJ, USA. Freshly boiled distilled water was used for the pharmaceutical preparations. Theophylline, diphenhydramine, ammonium chloride, menthol were gifted from Zafa Pharmaceutical Laboratories (Pvt) Limited. The buffer system used was $Na_2HPO_4$–$NaH_2PO_4$ (0.005 M), pH 7.0. The empty and drug filled glass (amber) and plastic amber (PVC) and semi-opaque (LDPE) cylindrical shape bottles, 120 mL, were procured from different pharmaceutical industries (Karachi). The details of various bottles of the pharmaceutical industries used in this study are given in table 2.

***Pharmaceutical preparation***

The pharmaceutical preparation in glass and plastic bottles contained a liquid preparation (cough syrup, pH 6.0 - 6.2) for evaluation.

***Composition of syrup***

The composition of cough syrup each 5mL contains Theophylline BP (32 mg), diphenhydramine BP (8 mg), ammonium chloride BP (30mg), menthol BP (0.98mL).

***Storage of drug filled bottles***

The properly sealed bottle samples of fresh pharmaceutical preparation were stored in a stability chamber (Model STC 410 Galvano Scientific, maintained at 30 ±1$^{o}$C, R.H. 65%) for a period of six months. After this period the bottles were emptied, thoroughly washed with distilled water, dried and the transmission characteristics recorded. The light transmission measurement on glass and plastic bottles was carried out

on a Schimatzu UV-visible recording spectrometer (model UV-160, Japan) according to the methods of BP (2016) and USP (2006).

***Sample preparation***

The bottle samples were prepared according to the description of BP (2016) and USP (2006).

***Method of light transmission measurement***

The glass bottles were cut into a suitable section size (10 mm wide and 35 mm long) with circular saw fitted with a wet abrasive wheel, such as carborundum or a bonded-diamond wheel. The plastic bottles were cut into suitable section size with the help of a blade and scissor. The sections representative of wall thickness of body part were selected and trimmed as suitable for mounting in a spectrophotometer. Before placing in the spectrophotometer holder, the glass and plastic sections were washed, dried and wiped thoroughly with a tissue. The sections were mounted with the aid of a forceps taking care to avoid leaving finger prints or other marks. The sections were placed in the spectrophotometer with its cylindrical axis parallel to the plane of the slit and approximately centered with respect to the slit in such a way that the light beam was perpendicular to the surface of the section and that the losses due to reflection are at a minimum. The transmission of the sections was measured with reference to air in the spectral region of 290 to 450 nm, continuously or at intervals of 20 nm. The observed light transmission for colored glass and plastic bottles for preparations that are used for solid and liquid oral dosage forms should not exceed 10% at any wavelength in the range from 290 nm to 450 nm, irrespective of the type and the capacity of the glass and plastic bottles.

***Photoprotection of riboflavin solution***

A $5\times10^{-5}$ M (18.82mg/L) aqueous solution of riboflavin was prepared at pH 7.0 (0.005M phosphate buffer). The solution was filled in transparent, amber glass, amber plastic (PVC) and semi-opaque (LDPE) bottles and exposed to visible light with a Philips HPLN 125 W high pressure mercury vapor florescent lamp (emission at 405 and 435 nm, the later band corresponding to the absorption maximum of riboflavin at 445 nm) (Ahmad and Rapson, 1990), fixed horizontally at a distance of 25 cm from the centre of the bottles. Samples of the photodegraded solution were removed at various intervals and subjected to spectrometer assay according to the method of Ahmad and Rapson (1990).

## RESULTS

***Transmission percentage of bottles***

The spectral characteristics of transparent glass, amber glass, amber plastic bottle and semi opaque plastic bottle was observed. In order to observe the spectral characteristic of the bottles used in this study along with that of the transparent glass, transmission spectra have been measured and are shown in fig.1.

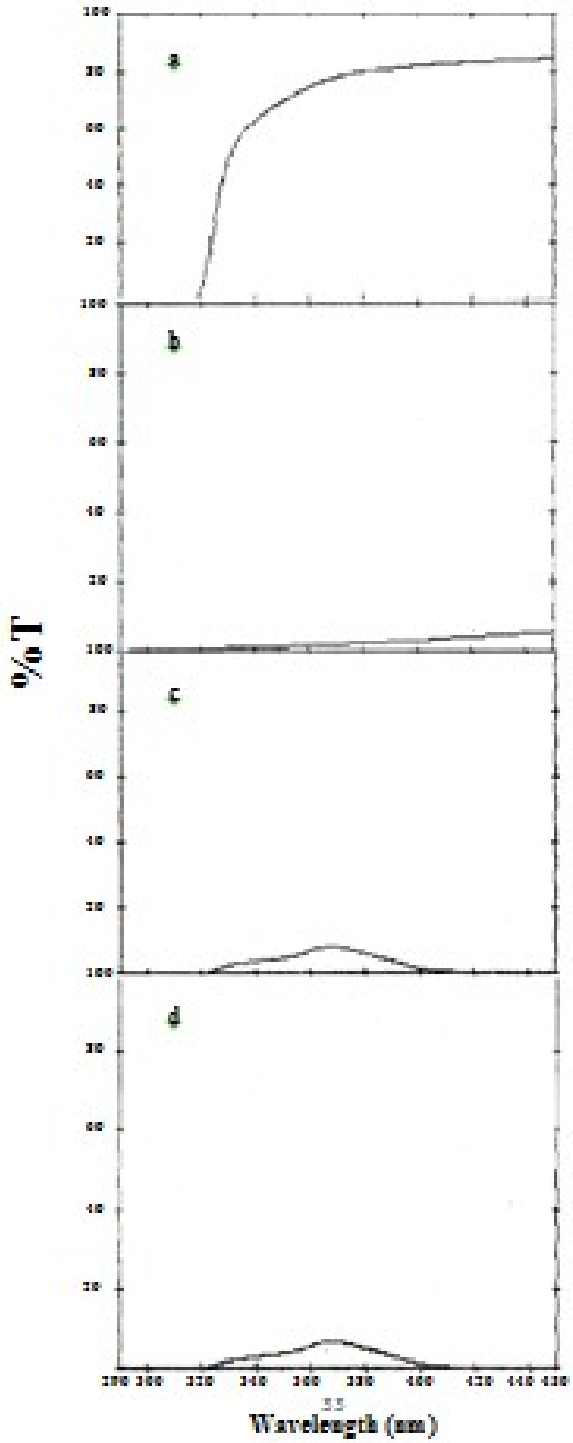


**Fig. 1**: Transmission spectra of bottles: (a) transparent glass, (b) semi-opaque LDPE plastic, (c) amber glass and (d) amber PVC plastic.

The calculation was on the basis of absorbance values at average thickness of bottles. For example, A ($\log I_o/ I_t$) at average thickness, b, of sample 1 (0.482) = 1.186 (since A

**Table 1**: Limits for glass type I, II and III and plastics classes I – VI Percentage of light transmission at any wavelength between 290 and 450 nm. British Pharmacopoeia (2016), United States Pharmacopeia (2016)

| Nominal size ( in mL) | Flame - sealed bottles | Closures-sealed bottles |
|---|---|---|
| 1 | 50 | 25 |
| 2 | 45 | 20 |
| 5 | 40 | 15 |
| 10 | 35 | 13 |
| 20 | 30 | 12 |
| 50 | 15 | 10 |

NOTE: Any bottle of a size intermediate to those listed above exhibits a transmission not greater than that of next larger size bottle listed in the table. For bottles larger than 50 mL, the limits for 50 mL apply. The observed light transmission for bottles of type NP glass and for plastic bottle for products intended for oral or topical administration does not exceed 10% at any wavelength in the range from 290 to 450 nm.

**Table 2**: Details of glass and plastic bottles (120 mL) used in this study

| a) Empty bottles | | | |
|---|---|---|---|
| Material | Type | Capacity | Quantity |
| Glass | Ambered | 120 mL | 10 |
| Plastic | Ambered | 120 mL | 10 |
| Plastic | Semi-opaque | 120 mL | 10 |
| Glass | Transparent | 120 mL | 01 |
| b) Drug filled bottles | | | |
| Material | Type | Capacity | Quantity |
| Glass | Ambered | 120 mL | 10 |
| Plastic | Ambered | 120 mL | 10 |
| Plastic | Semi-opaque | 120 mL | 10 |
| Glass | Transparent | 120 mL | 01 |

α b). Furthermore, the transmission (T) was calculated as T= antilog A (log $I_o$/ $I_t$) = antilog 1.186 = 15.35 = $I_o$ / $I_t$ or T = 100/ 15.35 = 6.5 %.

The light transmission characteristics of 10 empty amber glass bottles (120 mL) have been determined according to the BP/USP methods and were reported in table 3,whereas, light transmission characteristics of 10 drug filled amber glass bottles (120 mL) after storage for 6 months at room temperature (30±1°C) in the dark were reported in table 3.

The light transmission characteristics of empty amber plastic bottles are reported in table 4. Considering the transmission characteristics of the drug filled amber plastic bottles stored for 6 months, the thickness of the samples varied from 0.135-0.145 mm (av. 0.139 mm). The %T values of the samples for this thickness ranged from 8.7- 14.0 % table 4.

The semi-opaque plastic bottles are in considerable use for the packing and storage of drug products. The samples of these bottles showed a thickness of 0.425-0.479 mm (av. 0.456 mm) exhibiting transmittance values in the range of 1.1-2.4% table 5. An examination of the bottles filled with the drug and stored for 6 months showed thickness in the range of 0.468-0.482 mm (av. 0.471 mm) and gave a transmittance values in the range of 2.4-6.3%. For the average thickness of the bottles these values varied from 2.5-6.7% table 5. The % T values of all the bottles are within BP/ USP limits.

The interaction of bottles with drug is evaluated by filled drug bottle spectra. It has been observed there was changed in the absorbance in empty bottle and drug filled bottle. This interaction may effect on efficacy of drugs. In this study the increase in T% of drug filled glass bottles (table 3) may alter their photo protective efficacy of the bottles.

***Assay of riboflavin solution***

RF is a photosensitive drug. The values of photolysis of RF rate constant ($k_{obs}$) were noted in table 6. The values of $k_{obs}$ were determined by slope of the plot log concentration of RF versus time. Furthermore, the shelf-life was also calculated by the values of $k_{obs}$ of RF.

## DISCUSSION

### *Spectral characteristics of bottle*

The transparent glass starts transmitting light in the region of 320-450 nm with % T of 76.8% at 367nm (used in this study) and 84.2% at 450nm maximum in this region. These values indicate that transparent glass bottles are not suitable for the storage of photo labile drugs. In the case of semi- opaque LDPE plastic bottle, a% T of 2.1% at 367 nm and 5.7% at 450 nm has been observed with a gradual rise in %T in the 320-450 nm regions. The amber glass bottle gives a maximum % T of 8% at 367 nm and the amber PVC plastic bottle 7.2% at 367 nm. On the basis of these data, the semi- opaque plastic bottle is the most photo-protective bottle followed by amber PVC plastic and amber glass bottles (Karamer, 2006).

**Table 3**: Light Transmission Characteristics of Empty and Drug Filled Amber Glass Bottle[a]

| Empty Amber Glass Bottle Sample | Thickness (mm) | 367 nm (%)T | Absorbance (A) | 367nm (%)T | Filled Amber Glass Bottle Sample | Thickness (mm) | 367 nm (%)T | Absorbance (A) | 367 nm (%)T |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 0.502 | 5.8 | 1.236 | 6.5 | 1 | 0.480 | 9.8 | 1.008 | 12.1 |
| 2 | 0.510 | 3.4 | 1.468 | 4.1 | 2 | 0.412 | 11.2 | 0.950 | 9.4 |
| 3 | 0.502 | 6.1 | 1.214 | 6.9 | 3 | 0.480 | 13.1 | 0.882 | 15.2 |
| 4 | 0.500 | 8.2 | 1.086 | 9.0 | 4 | 0.440 | 11.0 | 0.958 | 10.7 |
| 5 | 0.492 | 2.4 | 1.619 | 2.6 | 5 | 0.445 | 20.4 | 0.690 | 20.4 |
| 6 | 0.422 | 3.0 | 1.522 | 1.9 | 6 | 0.424 | 15.7 | 0.804 | 14.3 |
| 7 | 0.490 | 8.8 | 1.055 | 9.2 | 7 | 0.468 | 12.5 | 0.903 | 13.9 |
| 8 | 0.415 | 2.0 | 1.698 | 1.1 | 8 | 0.428 | 12.6 | 0.899 | 11.6 |
| 9 | 0.488 | 4.6 | 1.337 | 4.9 | 9 | 0.426 | 11.6 | 0.935 | 10.6 |
| 10 | 0.500 | 6.2 | 1.207 | 6.9 | 10 | 0.458 | 13.8 | 0.860 | 14.6 |
| Average Thickness | 0.482 | | | | Average Thickness | 0.446 | | | |

**Table 4**: Light Transmission Characteristics of Empty and Drug Filled Amber Plastic Bottle (PVC)[a]

| Empty Amber Plastic Bottle Sample | Thickness (mm) | 367 nm (%)T | Absorbance (A) | 367 nm (%)T | Filled Amber Plastic Bottle Sample | Thickness (mm) | 367 nm (%)T | Absorbance (A) | 367 nm (%)T |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 0.142 | 1.6 | 1.795 | 1.7 | 1 | 0.145 | 9.2 | 1.036 | 10.2 |
| 2 | 0.140 | 1.9 | 1.721 | 2.0 | 2 | 0.135 | 10.9 | 0.962 | 9.8 |
| 3 | 0.142 | 1.8 | 1.720 | 1.9 | 3 | 0.140 | 10.4 | 0.982 | 10.7 |
| 4 | 0.140 | 4.2 | 1.376 | 4.2 | 4 | 0.140 | 8.5 | 1.070 | 8.7 |
| 5 | 0.142 | 4.6 | 1.337 | 4.9 | 5 | 0.140 | 10.1 | 0.995 | 10.3 |
| 6 | 0.136 | 5.3 | 1.275 | 4.8 | 6 | 0.135 | 14.2 | 0.847 | 13.5 |
| 7 | 0.140 | 7.2 | 1.142 | 7.3 | 7 | 0.140 | 10.9 | 0.962 | 11.0 |
| 8 | 0.140 | 7.3 | 1.144 | 7.2 | 8 | 0.141 | 13.6 | 0.866 | 14.0 |
| 9 | 0.140 | 7.8 | 1.107 | 7.8 | 9 | 0.144 | 10.4 | 0.982 | 11.3 |
| 10 | 0.142 | 3.9 | 1.408 | 4.0 | 10 | 0.139 | 12.2 | 0.913 | 12.0 |
| Average Thickness | 0.140 | | | | Average Thickness | 0.139 | | | |

**Table 5**: Light Transmission Characteristics of Empty and Drug Filled Semi-Opaque Plastic Bottle (LDPE)[a]

| Empty Semi-Opaque Plastic Bottle | Thickness (mm) | 367 nm (%) T | Absorbance (A) | 367 nm (%)T | Drug Filled Semi-Opaque Plastic Bottle | Thickness (mm) | 367 nm (%) T | Absorbance (A) | 367 nm (%) T |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 0.475 | 2.4 | 1.554 | 2.8 | 1 | 0.482 | 6.3 | 1.172 | 6.7 |
| 2 | 0.479 | 2.1 | 1.596 | 2.6 | 2 | 0.476 | 4.5 | 1.331 | 4.7 |
| 3 | 0.476 | 2.1 | 1.606 | 2.5 | 3 | 0.476 | 3.7 | 1.415 | 3.9 |
| 4 | 0.425 | 2.2 | 1.777 | 1.7 | 4 | 0.476 | 3.7 | 1.515 | 3.9 |
| 5 | 0.476 | 1.9 | 1.648 | 2.3 | 5 | 0.474 | 3.1 | 1.498 | 3.2 |
| 6 | 0.476 | 2.1 | 1.606 | 2.5 | 6 | 0.442 | 3.2 | 1.592 | 2.5 |
| 7 | 0.426 | 1.9 | 1.842 | 1.4 | 7 | 0.468 | 2.8 | 1.561 | 2.8 |
| 8 | 0.426 | 1.6 | 1.921 | 1.2 | 8 | 0.468 | 2.6 | 1.595 | 2.5 |
| 9 | 0.476 | 1.5 | 1.746 | 1.8 | 9 | 0.478 | 2.8 | 1.529 | 3.0 |
| 10 | 0.425 | 1.1 | 2.100 | 0.8 | 10 | 0.478 | 2.4 | 1.595 | 2.5 |
| Average Thickness | 0.456 | | | | Average Thickness | 0.471 | | | |

[a]Calculated on the basis of absorbance values at average thickness of bottles

**Table 6**: Apparent first-order rate constant ($k_{obs}$) for the photoprotection of riboflavin as a model compound in beakers and pharmaceutical glass and plastic bottles

| Bottles | $k_{obs} \times 10^4$, $min^{-1}$ | Shelf-life (min) | Stabilization Ratio |
|---|---|---|---|
| Pyrex Glass Beaker (100 mL) | 9.89 | 11 | – |
| Semi-Opaque Plastic Bottles | 0.83 | 1265 | 115 |
| Amber Plastic Bottles | 0.91 | 1153 | 105 |
| Amber Glass Bottles | 2.62 | 40 | 4 |
| Transparent Glass Bottles | 9.16 | 12 | 1.09 |

***Amber glass bottle***

The $\lambda_{max}$ in the 290 – 450 nm specified in BP/ USP occurred at 366-368 nm (avg. 367 nm) in all the samples and, therefore, the transmission measures have been made at 367 nm. The thickness of the uniform sections of the walls of the bottles varied from 0.415 - 0.510 mm (avg. 0.48 mm). Using the absorbance (A) of the %T values of the individual sample, % T values at the average thickness of the bottles have been calculated for comparison the values range from 1.1-9.2% at 367 nm, indicating the increase in %T values in the order of samples: 8 < 6 < 5 < 2 < 9 < 1 < 3 < 10 < 4 < 7.

Thus sample 8 has the lowest transmission and sample 7 has the highest transmission on the basis of an average thickness of the bottles. The evaluations of transmission characteristics of the samples shows that the %T values of these samples increase in the above order and the efficacy of the samples in inhibiting the light transmission would be in the reverse order. These results indicate that the various amber glass bottles available for the storage of drugs do not exhibit the same light transmission characteristics and may differ on the basis of their thickness and compositional variations (Campbell and Vallejo, 2015). The BP (2016) and (2006) limit for the transmission of colored light protecting glass bottles is within 10%. In the present case the %T values of the bottles lie in this range.

The thickness values of these bottles ranged from 0.412 – 0.480 mm (av. 0.446 mm) and the % T values at the average thickness varied from 9.4 -20.4%. These values show an increase in the transmission characteristics of the bottles not in the same order as observed for the empty bottles and are as follows: 2< 9< 4< 8< 1< 7< 6< 10<3<5

This could probably be due to the interactions of the cations of the iron and manganese oxides which catalyze oxidative reaction and may be extracted from the glass thereby increasing its transmission characteristics (Rehm, 1967). Thus an interaction of the drug ingredients with the glass components may change the transmission characteristics of the bottles and could be detrimental for the photosensitive drugs on storage.

***Amber plastic bottle (PVC)***

The thicknesses of the uniform section of these bottles are in the range of 0.136-0.142 mm (av. 0.140 mm) and the %T values for the average thickness are 1.7-7.8%. These values indicate that the %T of theses bottles increases in the order of samples: 1< 3 < 2 < 10 < 4 < 6 <5 < 8 <7< 9.

These values show that sample 1 followed by other samples in the above order give an increasing %T and are best in light protection in the reverse order. The difference in light transmission characteristics of the bottles is due to slight variations in thickness and composition of plastic material used to manufacture these bottles.

These values indicate that the filled plastic bottles show higher transmission than those of the empty bottles (table 4). This could be probably due to the interaction of coloring pigments of the plastic with the ingredient of the drug product during storage. Even micro quantities of chemically incompatible substance can alter the appearance of the drug product or plastic bottle (Croce *et al*., 1986) and thus increase the value of %T depends on the degree of interactions. This behavior suggests that the drug ingredients could damage the surface of the bottles and extract its components and thus increase the %T which could affect the stability of photosensitive drugs (Tonnesen, 2004).

***Semi-Opaque Plastic Bottle (LDPE)***

The %T values (table 5) for the average thickness of the bottles varied from 0.8 – 2.8 % and were in the order of samples: 10 < 8 < 7 < 4 < 9 <5 < 3 < 6 < 2 < 1

These values show an increase in %T of the samples indicating that sample 10 is the best in providing light protection and sample 1 has the highest %T for the bottles studied. However all the values are within the BP / USP limits of 10% T.

A difference between the %T values of the empty (table 5) and the drug filled semi-opaque plastic bottles (table 5) appears to be due to some interaction of the drug ingredients with the components of the bottles during storage. However, the increase in the transmission characteristics is relatively small and is within the range of BP/ USP limit. It is also less than that observed in the

case of amber glass and plastic bottles. The results of the present study on the transmission characteristics of different types of bottles shows that the semi-opaque plastic bottles are better than the amber plastic bottle which in turn are better than the amber glass bottles when filled with the same drug and stored for 6 months. It is important to consider that the efficiency of the bottles in light protection depends on thickness, composition of bottles, release of coloring agents and pigments, drug bottles interaction, storage condition and period and the degree of extraction coloring agents into the medium (Hahladakis *et al*., 2018). A comparison of the bottles of a single category and batch also becomes difficult due to thickness variation, manufacturing process, cost cutting and quality and sensitivity of bottle components to light (Adil and Moutawakil, 2012).

***Drug-container interaction***

An important factor in determining the efficacy of the bottles used for light protection is the nature and reactivity of the coloring material incorporated into the bottle to cut down the UV and visible radiation in the 290 – 450 nm regions (Robertson, 2012). The amber glass meets these specifications by the addition of $Fe_2O_3$ that could leach into the product (USP, 2006). Any change in the content of coloring material may alter the transmission characteristics of the bottle. The cations of metal oxides such as $Fe_2O_3$ and MnO, imparting color to the glass (Schott- Rohrglas, 2003) and the pigments such as azo dyes imparting color to the plastic (Jenke, 2003; Coltro and Borrghetti, 2007) or $TiO_2$ as a light scattering agent may interact with the formulation ingredients and be extracted in the solution (Jenke, 2001; Jenke, 2003; Jenke *et al*., 2006; Jenke, 2007). This may increase the amount of light being transmitted to the drug contents and enhance the rate of degradation of photosensitive drugs. The degree of interaction between the drug ingredients and the bottle components would depend on the chemical reactivity of the drug, medium characteristics, (for. e. g, pH, polarity, and solubilising capacity), the nature of coloring materials and storage conditions (Laschi *et al*., 2009). This problem could be minimized by the addition of relatively inert and largely insoluble coloring agents in the bottles material before manufacturing.

***Photo protective efficacy of containers using riboflavin solutions***

The photochemistry of riboflavin (vitamin $B_2$) (RF) is well established (Heelis, 1982; Heelis, 1991; Ahmad and Vaid, 2006; Ahmad *et al*., 2006) and in this study it has been used as a model compound to evaluate the photo protection efficacy of various bottles used. The photolysis of RF in aqueous solution (Ahmad *et al*., 2004; Hotzer *et al*., 2005) and in organic solvent (Ahmad *et al*., 2015) under UV and visible light (Ahmad *et al*., 2006) has been reported and the mechanism of these reactions has been discussed (Heelis, 1982; Heelis, 1991; Ahmad and Rapson, 1990). RF undergoes photo degradation by first-order kinetics (Ahmad *et al*., 2004; Ahmad *et al*, 2015b). In order to compare the photo protection efficacies of amber colored / semi-opaque bottles corresponding to an average thickness (table no 3-5), along with a transparent bottle filled with RF solutions visible absorption maximum, 444 nm (BP, 2016) were irradiated with visible light and the rate constants and shelf lives were determined. The data in table 6 has indicated that the bottles provide photo protection to RF solution in the order: Semi-opaque plastic > Amber plastic > Amber glass

This is in the same order as observed for the transmission characteristics of the empty and drug filled bottles as discussed above. These data indicate that RF photo protection depends on the amount of light being transmitted through a particular bottle, i.e., smaller the light transmission greater the photo protection to RF solutions. Thus in comparison to the transparent bottle, the other bottles is effective to the extent of 91.3% (semi-opaque LDPE), 90.5% (amber plastic) and 72.6% (amber glass) were provided photo protection to the drug. Therefore, semi-opaque plastic bottle appears to be most effective for the storage of photosensitive drugs.

## CONCLUSION

The transmission characteristics of different types of bottles used for the packaging and storage of drugs may influence the photo stability of the formulations. The greater the light transmission in a particular region the greater will be the possibility of photo degradation of the drug absorbing in that region. The light transmission depends upon the efficacy of the coloring component of the bottles. It has been observed and proved that photo protection efficacy of the transparent glass, yellow glass and PVC and HDPE and LDPE do not affect the stability of the drug packed if the bottles are of standard quality. The nature of drug like photo sensitive drug like riboflavin is more degraded in transparent glass and plastic bottle as compare to ambered, semi opaque and opaque LDPE and HDPE bottles because transparent glass and bottle absorb UV and visible light which may affect the drug stability and their shelf life as in case light sensitive drug riboflavin showing (12 mins) table no 6. It is important that the selection of the bottle must be according to the stability profile and nature of drug (Ahmad I, 2016). The interaction of these components with the drug and extraction in the solution would affect the light protective efficacy of the bottle and hence the photo protection of the drug. It is desirable to control the contents, thickness and the manufacturing process to maintain uniformity in the quality of the bottles for pharmaceutical industrial use (European Pharmacopoeia, 2015).

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