



## Preparation of coating solution

### Eudragit coating mixture

Eudragit L and S were prepared as a mixture in ratio 1:1 and 1:2 and coated with two concentrations 1% and 3% of each ratio.

The coating solution was prepared according to the Rohm pharma recommendations as shown in table (2) [16].

**Table 2: Composition of enteric coating solution**

Material	Amount (gm)
Eudragit L100 or S100	6
Isopropranol	115.7
Acetone	77.1
Dibutylphthalate	1.2
Semithicone	Few drops

### Shellac coating solution

Shellac 5 and 10% w/v was prepared in equal volume of acetone and isopropranol

### Tablets coating

The core tablets of the selected formula were coated by dipping method. Each tablet was held by forcipes and dipped in the coating lacquer in and out 15-20 times, the coat dried by steam of warm air between each dip [17].

### Characterization of prepared tablets

#### Weight Variation Test

The test was done for the 20 prepared tablets before and after coating for all formulas.

#### Hardness Test

The hardness of three tablets of the prepared formulas was determined individually using Monsanto hardness tester

#### Friability Test

This test was done by subjecting 10 tablets utilizing Roche friabilator that revolves at 25 rpm. Compressed tablets that lose a maximum of not more than 1% of their weight are generally considered acceptable according to pharmacopeia [18].

#### Drug Content

Assay was done by grinding 10 tablet in mortar and transfer the powder to a 1000-mL volumetric flask, 100 ml of 1 N sodium hydroxide was added, shake to disperse the powder and add 800 ml of methanol. The solution was sonicated for 15 min and stirred for 30 min, finally diluted with methanol to volume. Fifteen ml of the filtered solution transferred to a 25-mL volumetric flask, and diluted

with water up to the volume, then 25  $\mu$ L was injected to the HPLC system.

The chromatographic condition includes column L1 (4-mm  $\times$ 10-cm), flow rate 0.8 ml/min, temperature 40°C and UV 254 nm as a detector [18]. Mobile phase was prepared by mixing two Solutions (A 63ml: B 37ml)

**Solution A:** 2.0 g/L of dibasic ammonium phosphate solution. Adjust with phosphoric acid to a pH of 7.0  $\pm$  0.1.

**Solution B:** Methanol and isopropyl alcohol (13:2)

### In vitro drug release study

Drug release was studied for all tablet formulations pre and post coating tablets by USP apparatus II (paddle) and 900 ml was filled with the medium at 37 $\pm$ 0.5°C and the rotation was 100 rpm. The first two hours of dissolution was in 0.1N HCl (only for coated tablet), followed in phosphate buffer pH 6.8 for one hour and then complete the dissolution using phosphate buffer pH 7.5 At the end of the third hour (phosphate buffer pH 6.8) 20 ml of the medium was taken and replaced by 20 ml 2N NaOH and adjusted pH to 7.5[18].

### Fourier Transform Infrared Spectroscopy (FTIR)

Samples of MLX powder, MLX uncoated tablet and coated tablet was grinded, mixed with potassium bromide) then analyzed by FTIR spectroscopy from 4000-400  $\text{cm}^{-1}$

### Stability Study

The stability of the selected coated formulas FLS3 and FSh1 was studied at three different temperatures; 40, 50, and 60 °C for 16 weeks.

After an interval of four months, samples were withdrawn and tested for various physical tests (hardness, friability, uniformity of dosage unit and drug release study)[19].

### Statistical Analysis

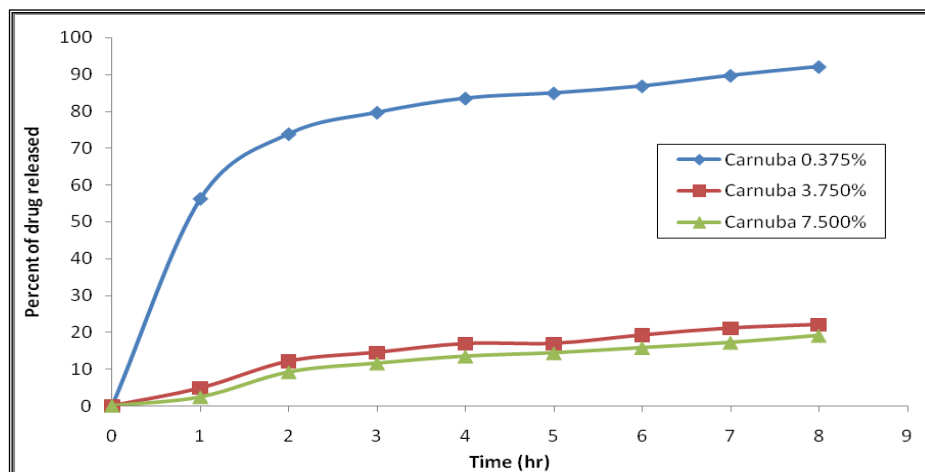
The results of the experiments are given as a mean of triplicate samples  $\pm$  standard deviation and were analyzed according to the one-way analysis of variance (ANOVA) to determine if the differences are statistically significant at ( $P < 0.05$ ).

## RESULTS AND DISCUSSION

### Effect of carnauba wax concentration on MLX release

Fig. (1) shows the effect of carnauba wax concentration on the release of MLX from formulas (F1-F3) which utilizes (7.5, 3.75 and 0.375%) of carnauba wax.

The results indicate that there is a significant differences ( $p < 0.05$ ) in the release of MLX when the carnauba wax concentration was changed. Although the release of drug was prolonged, but high percentage of drug was released in the first few hours.



**Fig. 1: Effect of carnauba wax concentration on release of MLX from CT tablets in phosphate buffer (pH6.8 and 7.5) at 37°C**

**Effect of ethylcellulose concentration on MLX release**

Formulas (F4-F7) were used to study the effect of ethyl cellulose concentrations (7.5, 5, 3.75, and 1.875%) on release of MLX from tablet.

The dissolution profiles shown in Fig. (2) indicate that increasing the concentrations of ethyl cellulose tend to decrease the drug release significantly differences ( $p < 0.05$ ). Same behavior of drug release from carnauba matrix was observed in these formulas recording burst release of drug.

**Effect of Eudragit RS concentration on MLX release**

The release of MLX from formulas F8-F12 which were formulated using Eudragit RS and lactose (diluent) in different concentrations (7.5, 5.625, 5, 3.75 and 1.875%) is shown in Fig. (3).

The results indicated that increasing the concentration of polymer tend to decrease the drug release significantly ( $p < 0.05$ ) this is due to decrease in the porosity with a concomitant increase in the tortuosity of matrix and this is in agreement with the results found in formulation of nicotine matrix[20]. Reasonable release profile for long time was obtained with 5%w/w Eudragit RS, thus this formula was selected as the best one and subjected to coating.

**Effect of Eudragit coating solutions constituent on MLX release**

The tablets (F10) with no signs of cracking or splitting or peeling was coated to prevent the release of drug in 0.1 N HCl and to target the drug to the colon.

Fig. (4) shows the effect of different concentrations 1% FLS1 and 3% FLS2 of Eudragit mixture L: S in ratio (1:1) in three pH medium (acidic 0.1NHCl, phosphate buffer 6.8, and 7.5).

**Effect of Shellac coating solutions constituent on MLX release**

Shellac is a natural polymer commonly used as an enteric coating material, Shellac coating solution was used to coat the selective formula 10 using two concentrations; 5% FSh1 and 10%.

Fig. (5) shows that there is no significant difference ( $P > 0.05$ ) between these two concentration which means that both concentrations provide the enteric properties for 2 hours, thus 5% concentration was preferred due to lower cost of formulation. This result is in agreement with the coating of theophylline pellets with shellac [21].

**Evaluation of prepared MLX Tablets**

The weight variation, drug content, hardness, and friability of the prepared tablets were within the accepted values.

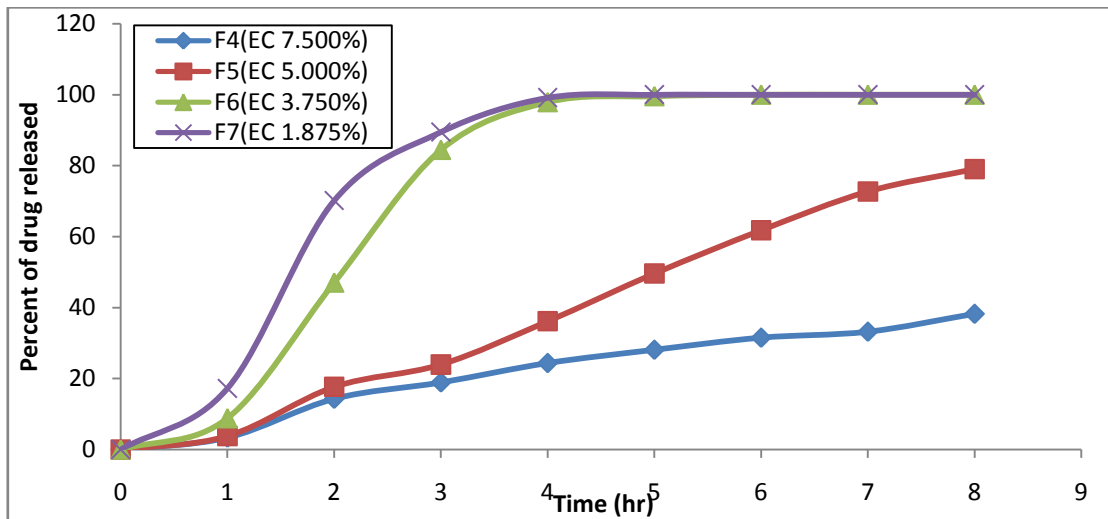


Fig. 2: Effect of ethylcellulose concentration on release of MLX from CT tablets in phosphate buffer (pH6.8 and 7.5) at 37°C

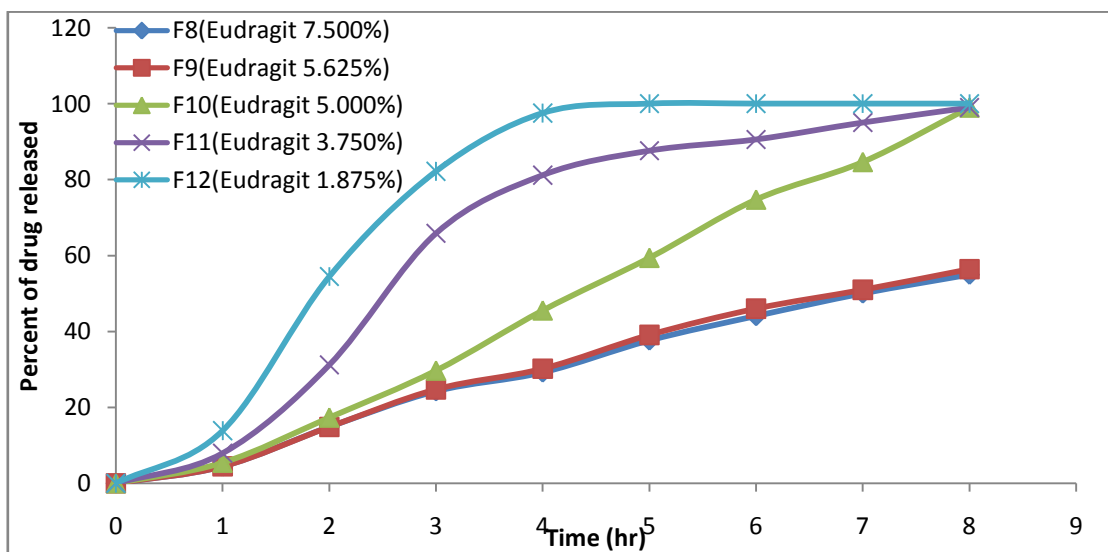


Fig. 3: Effect of Eudragit RS concentration on release of MLX from CT tablets in phosphate buffer (pH6.8 and 7.5) at 37°C

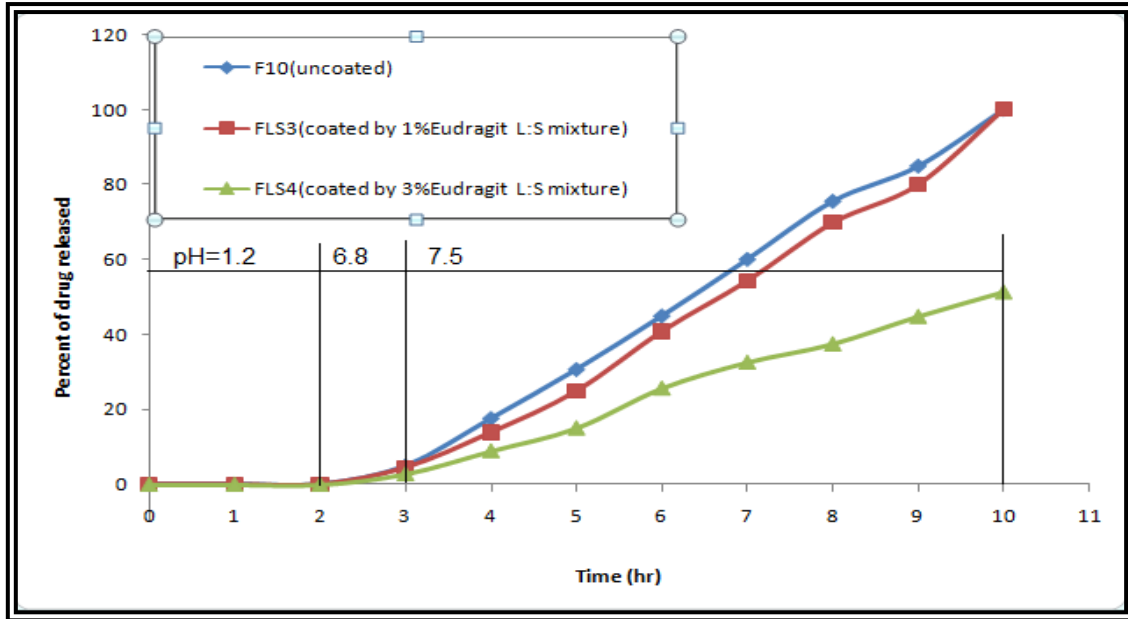


Fig. 4. Effect of Eudragit L: S (1:1) coating mixture concentration on release of MLX from C.T. tablet in 0.1NHCl, phosphate buffer (pH6.8 and 7.5) at 37°C.

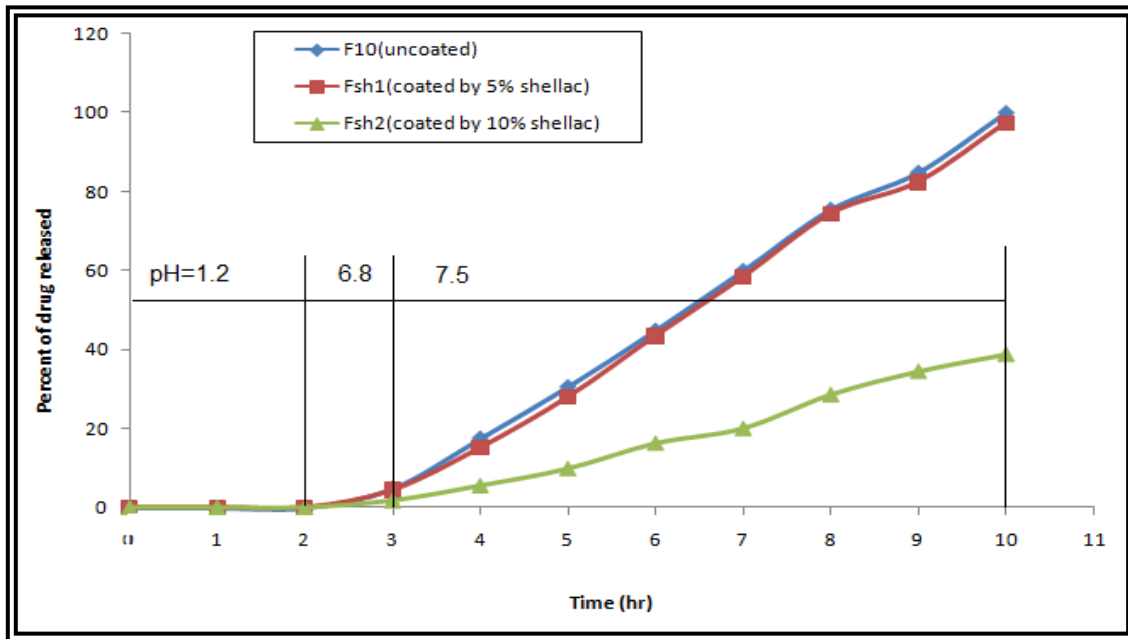


Fig. 5: Effect of shellac coating solution concentration on release of MLX from C.T. tablet in 0.1NHCl, phosphate buffer (pH6.8 and 7.5) at 37°C.

**Fourier Transform Infrared Spectroscopy (FTIR)**

The MLX coated and uncoated tablet exhibited similarity in the spectrum which indicated that the coating with Eudragit and shellac not affect the core tablet.

**Stability Study**

The degradation rate constants (K) at three temperatures were determined from the slope of each line, and these are summarized in table (3). Arrhenius plot was constructed to estimate the degradation rate constant (K<sub>25</sub>) at 25°C, the value of which was found to be 1 × 10<sup>-3</sup> week<sup>-1</sup>. This value was used to calculate the shelf life of the product by using the following equation;

$$T_{90\%} = 0.105/K_{25}$$

where t<sub>90%</sub> is the time required for a drug to lose 10% of its potency. The estimated shelf life of the selected formula was found to be 105

weeks or about 2years. Tablets inspected at the end of stability study exhibited no change in their appearance FLS3 and FSh1.

**Table 3: Degradation rate constants (K) for coated MLX CT tablets at different temperatures**

Temperature (°C)	K (week <sup>-1</sup> )
40	2 × 10 <sup>-3</sup>
50	4 × 10 <sup>-3</sup>
60	5 × 10 <sup>-3</sup>

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