PHARMACEUTICAL ELABORATION AND EVALUATION OF QUALITY CONTROL PARAMETERS FOR EXPIRED AND NON-EXPIRED ANTIBACTERIAL TABLETS (OFLOXACIN) ACCORDING TO I.P

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ABSTRACT

This study is predicted to target the standard of terminated drug and to assess whether or not quality of terminated medication deteriorates to what extent. This work is impressed by shelf-life extension program undertaken by North American nation Military and Defence unit. It'll conjointly facilitate in understanding efficiency of the terminated Formulation when the date of end and what parameters that area unit affected when end date area unit. It's been ascertained that not essentially when the expiration date the drug Loses its efficiency and efficaciousness. It'd show some ototoxic effects. This work focuses on qualitative analysis of terminated formulation with reference to non-expired one.

Keywords: Oflokem Quality Control Test, Evofox Quality Control Test, Ofloxacin.

I. INTRODUCTION

• What is EXPIRATION DATE?
The expiration date of a medicine indicates the date the manufacturer or health care provider guarantees the total efficiency and safety of a drug.

• What is SHELF LIFE?
The ICH defines time period because the period of time that a drug product is predicted to stay at intervals the approved shelf-life specification given that it’s keep underneath conditions outlined on the instrumentation label. It’s expected that the particular shelf-life specification can slightly exceed the projected tagged time period. Time period is variably influenced by storage conditions, like exposure to heat, light-weight and wet.

• Is there any distinction between time period and EXPIRATION DATE?
The term “shelf life” of a drug slightly differs from a drug’s “expiration date.” The amount period of your time typically relates to a drug’s quality over a mere period of time, whereas the expiration date relates to each quality and safety of a medicine at a selected purpose in time.

II. RATIONALE

This study is predicted to target the standard of terminated drug and to assess whether or not quality of terminated medication deteriorates to what extent. This work is impressed by shelf-life extension program undertaken by North American nation Military and defence unit. It'll conjointly facilitate in understanding efficiency of the terminated formulation when the date of end and what area unit parameters that area unit affected when end date

It has been ascertained that not essentially when the expiration date the drug loses its efficiency and efficaciousness. It'd show some ototoxic effects. This work focuses on qualitative analysis of terminated formulation with reference to non-expired one

III. OBJECTIVE

The major objectives of the current analysis area unit as printed below:

• Study the standard management parameters of formulation when end date.

• Comparison of internal control parameters of terminated and non-expired formulation.

• Analyze the standard of terminated medication supported its internal control tests.
Table 1. Ofloxacin Tablets

<table>
<thead>
<tr>
<th>Sr no.</th>
<th>Tablet name</th>
<th>Manufacturing Date</th>
<th>Expiry Date</th>
<th>Tablet manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>OFLOKEM 200mg IP</td>
<td>August 2021</td>
<td>July 2023</td>
<td>Alkem Laboratories Ltd</td>
</tr>
<tr>
<td></td>
<td>(non-expired)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>OFLOKEM 200mg IP</td>
<td>March 2020</td>
<td>April 2022</td>
<td>Alkem Laboratories Ltd</td>
</tr>
<tr>
<td></td>
<td>(expired)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### IV. DRUGS MONOGRAPH

1. Common name: - Ofloxacin
2. Class: - Quinolones
3. Therapeutic class: - Antibacterial agent
4. Chemical name: ±)-9-Fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1- piperazinyl)-7-oxo7H-pyrido[1,2,3-de]-1,4-benzoazine-6-carboxylic acid
5. Structural formula: -

![Structural formula of Ofloxacin](image)

6. Mol. Weight: - 361.37
7. Mol. Formula: - C18H20FN3O4
8. Melting Point: - 260-270°C
9. Appearance: - cream to pale yellow crystalline powder
10.Solubility: - Soluble in glacial acetic acid, sparingly soluble in Chloroform, slightly soluble in water, methanol, ethanol or acetone.
11.Stability and Storage: - OFLOXACIN is sterile in the unopened package. Store At 4° to 30°C. Tablets should be kept in well closed Container, protected from light.
12.Side effects: - Peripheral neuropathy, anxiety, chest pain, depression, Diarrhea, eye pain, fast heartbeat, dry skin, headache, Nausea, nightmares, runny nose, seizures, sore throat.
13.Warning: - Ofloxacin is not for injection into the eye.
15.Use: - Respiratory tract infection.
   - Skin infection.
   - GI infection.
   - Anthrax
   - Mycobacterial infection (TB).
   - Typhoid fever.
16.Additional information: -
A] Strength In current WHO model list of essential medicines: - 200mg, 400mg.
B] Strength in current WHO model list of essential medicines for children: - 200mg, 400mg.

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### EXPERIMENTAL WORK
- Assay (Titration) of Ofloxacin drug
- Dissolution test of OFX tablets (EVIFLOX and OCILOX)
- Friability test
• Solubility
• Weight variation
• Disintegration test
• Hardness test
• Description (size, shape, thickness, diameter, color, odor)

PROCEDURE

ASSAY OFLOXACON TABLET (OCILOX 200 mg-Expired and EVIFLOX 200 mg- non-expired)

1. Twenty tablets each of expired and non-expire tablets were weighed and ground to fine powder.
2. Tablet powder equivalent to 200 mg of drug was transferred to 100 mL volumetric flask and it is dissolved and made up to mark with 0.1 N Hydrochloric acid.
3. The solution was filtered through Whatmann filter paper No. 41 and it is suitably diluted to obtain a solution having a concentration of 10 µg/ml.
4. This solution was analyzed by UV spectrophotometric method at the wavelength of 293 nm and the concentration of OFX was calculated in the tablet formulation.

I.P. Limit: The test is valid if the relative standard deviation is not more than 2.0 percent from the stated amount of C18H20FN3O4 in the tablet formulation.

V. DISSOLUTION TEST OF OFLOXACIN TABLETS

Apparatus No.1 (I.P)
Medium: 900 mL of 0.1 M hydrochloric acid (HCl)
Speed and time: 50 rpm and 30 minutes

• Preparation of 0.1 M hydrochloric acid (Dissolution medium):
  1. Take about 100 mL of distilled water in a cleaned and dried 1000 mL volumetric flask.
  2. Add about 8.5 mL of concentrated hydrochloric acid with continuous stirring.
  3. Add about 700 mL of distilled water, mix and allow to cool to room temperature.
  4. Make up the volume to 1000 mL using distilled water.
  5. Mix the solution thoroughly to obtain 0.1 N Hydrochloric Acids.
  6. Accordingly prepare 5000 mL of dissolution medium.

• Procedure for dissolution testing of tablets:
  1. Place 900 mL of 0.1 N HCl (dissolution medium), free from dissolved air, into the four vessels of the apparatus.
  2. Assemble the apparatus and warm the dissolution medium to 36.5° to 37.5°.
  3. When the apparatus is ready for the test, place One tablet in each of the vessels and let 1 Vessel remain as the Blank.
  4. Operate the apparatus immediately at the speed of rotation specified in the individual monograph (50 Rpm).
  5. Within the time interval stated, withdraw a specimen (5 mL) a zone midway between the surface of the dissolution medium and the top of the rotating blade and replace a Volume of the dissolution medium equal to the volume of Sample withdrawn.
  6. Filter the sample solution promptly using a Whatmann filter paper and perform the analysis using UV spectrophotometer at the wavelength of 293 nm and calculate the amount of dissolved OFX [C18H20FN3O4] in solution as a percentage of the stated amount.

I.P Limit: Not less than 75 percent of the stated amount of C18H20FN3O4 in the medium.

VI. FRIABILITY TEST OF OFLOXACIN TABLETS

1) De-dust the tablets carefully and weigh accurately the required number of tablets.
2) Place the tablets in the drum and rotate it 100 times. remove the tablets, remove any loose dust from them and weigh them accurately.
3) The test is run only once unless the results are difficult to interpret or if the weight loss is greater than the targeted value, in which case, the test is repeated twice and the mean of the three tests is determined.
4) A maximum loss of weight (from a single test or from the mean of the three tests) not greater than 1.0 % is acceptable for most tablets.
5) If obviously cracked, chipped or broken tablets are present in the sample after tumbling, the sample fails the test. For each formulation, the friability was determined using Roche type friabilator.

6) Tablets were weighs and tested at a speed of 25 rpm for 4 minutes. After removing of dusts, tablets were re-weighed and friability percentage was calculated using the

\[
\% \text{friability} = \frac{\text{Tablet weight before friability} - \text{Tablet weight after friability}}{\text{Tablet weight after friability}} \times 100
\]

**NOTE:** If the size or shape of the tablet causes irregular tumbling, adjust the drum base so that it forms an angle of about 10° with the horizontal and the tablets do not bind together when lying next to each other, which prevents them from falling freely.

**VII. WEIGHT VARIATION TEST FOR OFLOXACIN TABLETS**

Weight variation was carried out to ensure that, each of tablets contains the proper amount of drug.

The test was carried out by weighing 20 tablets individually using analytical balance, then calculating the average weight, and comparing the individual tablet weight to the average.

**Table 2. Weight variation standard chart**

<table>
<thead>
<tr>
<th>Sr.no</th>
<th>Average no. Of tables (mg)</th>
<th>Maximus percentage difference allowed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>80mg or less.</td>
<td>+(-) 10.0</td>
</tr>
<tr>
<td>2</td>
<td>More than 80 mg or less than 250 mg.</td>
<td>+(-) 7.5</td>
</tr>
<tr>
<td>3</td>
<td>250 mg or more</td>
<td>+(-) 5.0</td>
</tr>
</tbody>
</table>

**VIII. DISINTEGRATE TEST FOR OFLOXACIN TABLETS**

This test determines whether dosage forms such as tablets, capsules, boluses, pessaries and suppositories disintegrate within a prescribed time (disintegration time) when placed in a liquid medium under the prescribed experimental condition.

**Basic steps followed in Disintegration test:**

1. The disintegration apparatus, described in I.P was used for the study. It contains 2 basket rack assembly.
2. Each basket rack assembly consists of 6 glass tubes that are 3 inches long, open at the top and held against 10 mesh screens at the bottom. (We have added 3 tablets in one of the basket racket in assembly).
3. Each tablet was placed in each tube, and the basket rack was positioned in 1-L beaker of distilled water.
4. The 37±2 °C was maintained throughout the study.

**IX. HARDNESS TEST FOR OFLOXACIN TABLETS**

Tablet hardness is defined as the load required for crushing or fracture a tablet placed on its edge. Sometimes it is also termed as tablet crushing strength.

1. The hardness test was performed using MONSANTO HARDNESS TESTER.
2. The instrument measures the force required to break the tablet when the force generated by anvils to the tablet.
3. The tablet was placed between two Anvils; force applied to the anvils, and the crushing strength that just causes the tablet to break was recorded. Crushing strength test was performed on 3 tablets from each formulation namely Oflokem 200 mg IP.
4. (expired) and Ollokem 200 mg IP (non-expired).

**INSTRUMENTS**

- **Fig 1**: Analytical Weighing Balance
- **Fig 2**: Disintegration Test Apparatus
- **Fig 3**: Monsatto Hardness Tester Apparatus
- **Fig 4**: Dissolution Test Apparatus
- **Fig 5**: Titration test apparatus
- **Fig 6**: Vernier Caliper
X. OBSERVATIONS AND RESULT

Description of tablet

Parameter:
- **Color**: White
- **Shape**: Round, biconvex
- **Odor**: Characteristic
- **Size in mm**:
  - **Thickness**: 4.9 mm
  - **Diameter**: 9.9 mm

TITRATION

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Burette readings</th>
<th>Titration 1</th>
<th>Titration 2</th>
<th>Titration 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Initial readings</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>2.</td>
<td>Final readings</td>
<td>10.1</td>
<td>10.1</td>
<td>10.1</td>
</tr>
</tbody>
</table>

TITRATION

<table>
<thead>
<tr>
<th>Sr.no.</th>
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<th>Titration 2</th>
<th>Titration 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Initial readings</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>2</td>
<td>Final readings</td>
<td>11.2</td>
<td>11.3</td>
<td>11.6</td>
</tr>
</tbody>
</table>

DISSOLUTION

<table>
<thead>
<tr>
<th>Time (Min)</th>
<th>Sample A % R</th>
<th>Sample B % R</th>
<th>Sample C % R</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>60.04</td>
<td>78.75</td>
<td>89.62</td>
</tr>
<tr>
<td>10</td>
<td>80.44</td>
<td>83.57</td>
<td>93.13</td>
</tr>
<tr>
<td>15</td>
<td>93.47</td>
<td>86.9</td>
<td>100.0</td>
</tr>
<tr>
<td>20</td>
<td>92.12</td>
<td>94.16</td>
<td>99.33</td>
</tr>
<tr>
<td>30</td>
<td>95.1</td>
<td>92.5</td>
<td>100.7</td>
</tr>
</tbody>
</table>

Dissolution

<table>
<thead>
<tr>
<th>Time (Min)</th>
<th>Sample A % C. R</th>
<th>Sample B % C. R</th>
<th>Sample C % C. R</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>52.94</td>
<td>59.89</td>
<td>53.1</td>
</tr>
<tr>
<td>10</td>
<td>74.06</td>
<td>78.89</td>
<td>80.17</td>
</tr>
<tr>
<td>15</td>
<td>79.06</td>
<td>85.86</td>
<td>84.40</td>
</tr>
<tr>
<td>20</td>
<td>84.19</td>
<td>95.23</td>
<td>89.40</td>
</tr>
<tr>
<td>30</td>
<td>86.69</td>
<td>84.14</td>
<td>84.81</td>
</tr>
</tbody>
</table>

FRIABILITY

<table>
<thead>
<tr>
<th>FRIABILITY (%)</th>
<th>Oflokem 200mg (expired)</th>
<th>Oflokem 200mg (non-expired)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.31</td>
<td></td>
<td>0.30</td>
</tr>
</tbody>
</table>

Note: Both the tablet showed friability below 1%. This is under limit of friability which states that none of tablet should be having friability more than 1%.
Weight variation

Table 7. Observation table for wt. variation Of Ofлокем (non-expired).

<table>
<thead>
<tr>
<th>Sr. no.</th>
<th>Weight of tablets (in gm.)</th>
<th>Sr. no.</th>
<th>Weight of Tablet (in gm.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.33</td>
<td>11</td>
<td>0.31</td>
</tr>
<tr>
<td>2</td>
<td>0.32</td>
<td>12</td>
<td>0.33</td>
</tr>
<tr>
<td>3</td>
<td>0.33</td>
<td>13</td>
<td>0.33</td>
</tr>
<tr>
<td>4</td>
<td>0.31</td>
<td>14</td>
<td>0.32</td>
</tr>
<tr>
<td>5</td>
<td>0.32</td>
<td>15</td>
<td>0.32</td>
</tr>
<tr>
<td>6</td>
<td>0.31</td>
<td>16</td>
<td>0.32</td>
</tr>
<tr>
<td>7</td>
<td>0.36</td>
<td>17</td>
<td>0.31</td>
</tr>
<tr>
<td>8</td>
<td>0.32</td>
<td>18</td>
<td>0.30</td>
</tr>
<tr>
<td>9</td>
<td>0.33</td>
<td>19</td>
<td>0.34</td>
</tr>
<tr>
<td>10</td>
<td>0.32</td>
<td>20</td>
<td>0.34</td>
</tr>
</tbody>
</table>

Table 8. Observation table for wt. Of Ofлокем (expired).

<table>
<thead>
<tr>
<th>Sr. no.</th>
<th>Weight of tablets (In gm.)</th>
<th>Sr.no.</th>
<th>Weight of tablets (In gm.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.33</td>
<td>11</td>
<td>0.33</td>
</tr>
<tr>
<td>2</td>
<td>0.35</td>
<td>12</td>
<td>0.32</td>
</tr>
<tr>
<td>3</td>
<td>0.33</td>
<td>13</td>
<td>0.33</td>
</tr>
<tr>
<td>4</td>
<td>0.31</td>
<td>14</td>
<td>0.33</td>
</tr>
<tr>
<td>5</td>
<td>0.33</td>
<td>15</td>
<td>0.32</td>
</tr>
<tr>
<td>6</td>
<td>0.32</td>
<td>16</td>
<td>0.32</td>
</tr>
<tr>
<td>7</td>
<td>0.32</td>
<td>17</td>
<td>0.32</td>
</tr>
<tr>
<td>8</td>
<td>0.32</td>
<td>18</td>
<td>0.33</td>
</tr>
<tr>
<td>9</td>
<td>0.32</td>
<td>19</td>
<td>0.32</td>
</tr>
<tr>
<td>10</td>
<td>0.33</td>
<td>20</td>
<td>0.32</td>
</tr>
</tbody>
</table>

Percentage weight variation = \[ \frac{\text{Individual weight} - \text{Average weight}}{\text{Average weight}} \times 100 \]

XI. RESULT AND DISCUSSION

1. The test was performed according to I.P
2. For Ofлокем, the average percentage deviation of all tablets was in the range of 0.306 g to 0.339 g.
3. Hence according to the table 5 only three tablets are out of limit.
4. For, Ofлокем, the average % deviation of all the tablets were in the range of 0.308 g to 0.314 g.
5. Hence according to table 6 we can say that three tablets are out of limit.
6. Hence tablets have passed the weight variation test.

Disintegration test

- The disintegration time of film coated tablet namely Evoflox 200 mg IP (expired) and EVIFLOX 200 mg (non-expired) were found to be complied within the limits of Indian pharmacopoeia which states that time required for tablet to disintegrate should be NMT 30 min for film coated tablets.
- In case of comparative study, Evoflox (expired) tablet has disintegrated at much faster rate than Evoflox (non-expired) tablet.
Table 9. Disintegration for expired a non-expired tablet

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Disintegration Time (minutes)</th>
<th>Limits as per IP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Evoflox 200 mg IP (Expired)</td>
<td>Evoflox 200 mg IP (non-expired)</td>
</tr>
<tr>
<td>1</td>
<td>1 min 25 sec</td>
<td>15 min</td>
</tr>
<tr>
<td>2</td>
<td>1 min 45 sec</td>
<td>15 min 39 sec</td>
</tr>
<tr>
<td>3</td>
<td>1 min</td>
<td>14 min 19 sec</td>
</tr>
</tbody>
</table>

NMT 30 minute in water with disc for film coated tablets

HARDNESS TESTING
The hardness test of the above two tablet formulation namely OCILOX 200 mg IP (expired) and Oflokem 200 mg IP (non-expired) resulted in hardness of less than 4-6 kg/cm² and thus both of the tablet does not comply with the limits of IP.

Table 10. Hardness results for expired and non-expired tablet

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Hardness test (kg/cm²)</th>
<th>Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.5</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>2.5</td>
<td>1</td>
</tr>
<tr>
<td>Average</td>
<td>2</td>
<td>1.33</td>
</tr>
</tbody>
</table>

4-6(kg / cm²)

XII. CONCLUSION

• To conclude, we can say that the following evaluation test of tablets such as description, weight variation, hardness, friability, when compared of both the tablets namely Oflokem (expired) and Oflokem (non-expired), there was negligible difference among these tests of the tablet.

• On the other hand, some test such as Dissolution and Disintegration showed a major difference when results of Oflokem (expired) and Oflokem (non-expired) were compared.

• Thus, not a major difference between the results was observed however it may vary upon the other factors such as storage conditions, manufacturing conditions etc.

• The stability and quality of the expired products can only be assured by periodic testing and the evaluation of the expired medicine.

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XIII. REFERENCE


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