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UNIVERSITY OF RUHUNA – FACULTY OF ALLIED HEALTH SCIENCES
DEPARTMENT OF PHARMACY
FOURTH BPHARM PART II EXAMINATION – OCTOBER/NOVEMBER 2022
PH 4223 QUALITY CONTROL – SEQ
TIME: TWO HOURS

INSTRUCTIONS

- There are three parts in this paper (Part A, Part B and Part C).
- Answer all questions.
- No paper should be removed from the examination hall.
- Do not use any correction fluid.
- Use illustrations where necessary.

PART A

01.

1.1 Define the term "quality risk management". (***15 marks***)

1.2 Answer following questions based on essential aspects of GMP related to pharmaceuticals.

1.2.1 State the role of self-inspection in the quality management system. (***15 marks***)

1.2.2 Briefly describe the types of self-inspections conducted by companies. (***15 marks***)

1.2.3 State three purposes of good documentation practices. (***15 marks***)

1.3 In vivo - in vitro correlation of the assay of active pharmaceutical ingredient is critically important for sustained release products. Briefly explain the reasons for it. (***20 marks***)

1.4 Briefly explain five physical factors that should be considered when selecting materials for the construction of pharmaceutical machinery and equipment. (***20 marks***)

02.

2.1 *"Quality assurance, good manufacturing practices and Quality Control are interrelated aspects of Quality Management"*. Justify this statement. (***30 marks***)

2.2 Answer below questions using the provided monograph of Diclofenac sodium Extended-Release (ER) tablets.

2.2.1 State the name of the active pharmaceutical ingredient with upper and lower limits of the content. (***15 marks***)

2.2.2 List down the main tests that should appear in the finished product certificate of analysis (CoA) of Diclofenac sodium Extended-Release (ER) tablets. (***15 marks***)

2.2.3 Comment on the packaging and storage requirements of the Diclofenac sodium ER tablet. (***15 marks***)

2.3 Briefly explain five reasons for performing bioassays for pharmaceutical products instead of conducting chemical assays. (***25 marks***)

PART B

03.

3.1 Differentiate between "content uniformity" and "assay test" of a pharmaceutical dosage form. (***10 marks***)

3.2 "The determination of sucrose concentration is essential in quality control testing of syrups". Briefly describe the assay of active ingredients for syrups. (***25 marks***)

3.3

3.3.1 State two importance of performing friability test as a parameter in quality control testing. ***(10 marks)***

3.3.2 Briefly discuss the methods used to assess the friability with acceptance criteria/ reference limits. ***(20 marks)***

3.4 Write a short note on "evaluation of in-vitro disintegration of solid dosage forms". ***(35 marks)***

PART C

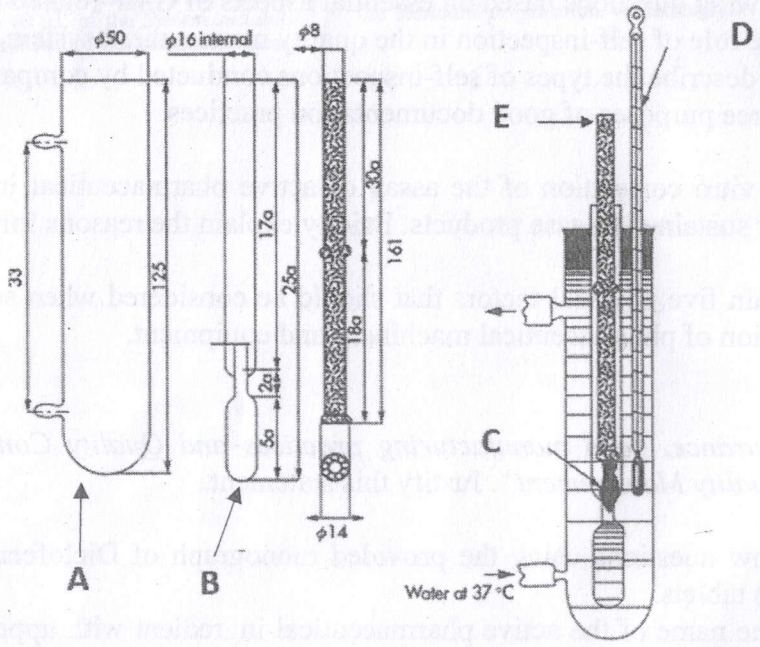
04.

4.1 Define the term "liquefaction time". ***(10 marks)***

4.2

4.2.1 Name the apparatus given below. ***(05 marks)***

4.2.2 Identify the A, B, C, D and E parts of the given apparatus. ***(15 marks)***



4.3

4.3.1 Define the term "packaging line". ***(05 marks)***

4.3.2 As a quality control manager of a new pharmaceutical company, you are asked to design a packaging area. Briefly describe four factors that you would consider when designing a packaging area. ***(30 marks)***

4.4

4.4.1 List three material that are used for primary packaging of medicines. ***(10 marks)***

4.4.2 Assume that your pharmaceutical company is planning to introduce new multivitamin soft gelatin capsule to the market. As a packaging manager, you have to select a suitable primary package for the product. Briefly describe five factors that you would consider when choosing packaging material/s for the drug package? ***(25 marks)***

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Diclofenac Sodium Extended-Release Tablets

» Diclofenac Sodium Extended-Release Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of diclofenac sodium ($C_{14}H_{10}Cl_2NNaO_2$).

Packaging and storage—Preserve in well-closed containers. Store at controlled room temperature, and protect from light.

Labeling—When more than one *Dissolution Test* is given, the labeling states the *Dissolution Test* used only if *Test 1* is not used.

USP Reference standards ⟨11⟩—*USP Diclofenac Sodium RS. USP Diclofenac Related Compound A RS.*

Identification—

A: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay.*

B: *Thin-Layer Chromatographic Identification Test* ⟨201⟩—

Solvent system: methanol, toluene, glacial acetic acid (40 : 60 : 0.5).

Test solution—Finely powder not fewer than 10 Tablets. Accurately weigh a portion of the powder, equivalent to about 50 mg of diclofenac sodium, and transfer to a 25-mL volumetric flask. Add about 15 mL of methanol, sonicate for 10 minutes, shake by mechanical means for 10 minutes, dilute with methanol to volume, and mix. Centrifuge this solution, and use the clear supernatant as the *Test solution.*

Standard solution—Accurately weigh about 50 mg of USP Diclofenac Sodium RS into a 25-mL volumetric flask. Add 10 mL of methanol, shake by mechanical means for 10 minutes, dilute with methanol to volume, and mix.

Change to read:

Dissolution ⟨711⟩—

TEST 1—

Medium: 0.05 M phosphate buffer, pH 7.5; 900 mL.

Apparatus 2: 50 rpm; use wire sinkers.

Times: 1, 5, 10, 16, and 24 hours.

Procedure—Determine the amount of $C_{14}H_{10}Cl_2NNaO_2$ dissolved by employing UV absorption at the wavelength of maximum absorbance at about 276 nm on filtered portions of the solution under test, suitably diluted with *Medium,* if necessary, in comparison with a Standard solution having a known concentration of USP Diclofenac Sodium RS in the same *Medium.*

Tolerances—The percentages of the labeled amount of $C_{14}H_{10}Cl_2NNaO_2$ dissolved at the times specified conform to *Acceptance Table 2.*

Time (hours)	Amount dissolved
1	between 15% and 35%
5	between 45% and 65%
10	between 65% and 85%
16	between 75% and 95%
24	not less than 80%

TEST 2—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2.*

Medium, Apparatus, and *Procedure*—Proceed as directed for *Test 1.*

Times: 1, 2, 4, 6, and 10 hours.

Tolerances—The percentages of the labeled amount of $C_{14}H_{10}Cl_2NNaO_2$ dissolved at the times specified conform to *Acceptance Table 2.*

Time (hours)	Amount dissolved
1	not more than 28%
2	between 20% and 40%
4	between 35% and 60%
6	between 50% and 80%
10	not less than 65%

TEST 3—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3.*

Medium and *Procedure*—Proceed as directed for *Test 1.*

Apparatus 1: 100 rpm.

Times: 2, 4, 8, and 16 hours.

Tolerances—The percentages of the labeled amount of $C_{14}H_{10}Cl_2NNaO_2$ dissolved at the times specified conform to *Acceptance Table 2.*

Time (hours)	Amount dissolved
2	between 22% and 42%
4	between 34% and 61%
8	between 52% and 82%
16	not less than 73%

•TEST 4—If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 4.*

Medium and *Procedure*— Proceed as directed for *Test 1.*

Apparatus 1: 100 rpm.

Times: 2, 4, 8, and 16 hours.

Tolerances—The percentages of the labeled amount of $C_{14}H_{10}Cl_2NNaO_2$ dissolved at the times specified conform to *Acceptance Table 2.*

Time (hours)	Amount dissolved
2	between 20% and 40%
4	between 35% and 55%
8	between 60% and 85%
16	not less than •85%• (RB 1-Mar-2010)

• (RB 1-Mar-2009)

Uniformity of dosage units ⟨905⟩: meet the requirements.

Assay—[NOTE—Protect the *Assay preparation, Standard preparation,* and *System suitability solution* from light.]

Diluent: a mixture of acetonitrile and water (43 : 57).

0.05 M Monobasic potassium phosphate buffer—Dissolve 6.8 g of monobasic potassium phosphate in 950 mL of water, adjust with dilute phosphoric acid or dilute potassium hydroxide solution to a pH of 4.0 ± 0.05, dilute with water to 1 L, and mix.

Mobile phase—Prepare a filtered and degassed mixture of acetonitrile, *0.05 M Monobasic potassium phosphate buffer,* and tetrahydrofuran (43 : 57 : 2). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Diclofenac related compound A solution—Dissolve an accurately weighed quantity of USP Diclofenac Related Compound A RS in *Diluent,* and quantitatively dilute with *Diluent* to obtain a solution having a known concentration of about 200 µg per mL.

Standard preparation—Dissolve an accurately weighed quantity of USP Diclofenac Sodium RS in *Diluent,* and quantitatively dilute with *Diluent* to obtain a solution having a known concentration of about 200 µg per mL.

System suitability solution—Transfer 10 mL of the *Standard preparation* and 5 mL of *Diclofenac related compound A solution* to a 20-mL volumetric flask. Dilute with *Diluent* to volume, and mix.

Assay preparation—Powder not fewer than 20 Tablets, and transfer an accurately weighed portion of the powder, equivalent to about 100 mg of diclofenac sodium, to a 100-mL volumetric flask, add about 50 mL of *Diluent,* sonicate for about 15 minutes, then shake by mechanical means for 15 minutes. Add a few drops of methanol to remove the foam, dilute with *Diluent* to volume, and mix. Transfer 10.0 mL of the supernatant to a 50-mL volumetric flask, dilute with *Diluent* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 15-cm column that contains 5-µm packing L1. The flow rate is about 1.5 mL per minute. Inject 40 µL of the *System suitability solution* into the chromatograph, and record the peak responses as directed for *Procedure:* the relative retention times are about 0.9 for diclofenac related compound A and 1.0 for diclofenac; and the resolution, *R,* between the diclofenac peak and the diclofenac related compound A peak is not less than 2.0. Inject 20 µL of the *Standard preparation* into the chromatograph, and record the peak responses as directed for *Procedure:* the tailing factor of the diclofenac peak is not more than 2.0; and the relative standard deviation of the diclofenac peak for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the area responses for the major peaks. Calculate the quantity, in mg, of diclofenac sodium ($C_{14}H_{10}Cl_2NNaO_2$) in the portion of Tablets taken by the formula:

$$500C(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Diclofenac Sodium RS in the *Standard preparation;* and r_U and r_S are the diclofenac peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.