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COMPARATIVE STUDY OF IN-PROCESS AND FINISHED PRODUCTS QUALITY CONTROL TEST FOR TABLET AND CAPSULES ACCORDING TO PHARMACOPOEIAS

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ABSTRACT

The goal of all Pharmaceutical industry is to make a good quality product and for this it is necessary to allow In-Process Quality Control (IPQC) Approaches. In-process quality control tests are done before the manufacturing process is completed. The function of in-process controls is to monitor and if necessary, adaptation of the manufacturing process to achieve the required specification. This may incorporate control of equipment and environment too. In-process materials should be tested for their physical parameters and its quality attributes which are later approved or rejected by the quality control department. The reason of IPQC is to deliver a cumulative finished product by avoiding or eliminating mistakes at every stage in production. The objective of this study is the comparison of In-process quality control test of India Pharmacopoeia, British Pharmacopoeia and the United state Pharmacopoeia. It was observed from various studies that quality control tests for tablet and capsule listed in different pharmacopoeias have slight similarities and differences.

Key words: *In-process quality control, Pharmaceutical tablets, Pharmaceutical Capsule, Pharmacopoeia*

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INTRODUCTION:

Quality is a broad term which includes suitability of drugs and products for their utilization which is decided by their efficiency and safety, according to label claim, or as promoted or publicized, their conformity to specifications about identity, purity and other characteristics. Quality gives importance to test the product for defects and reporting the same to the management. Management makes the decision to investigate or deny the release. According to the International Standard of Organization (ISO) quality control is the operational techniques and activities that are used to fulfil requirements for quality. With the help of In-process quality control producer can be able to follow all changes that occur during applied technological producers. Because of In-process quality control for the entire products producer fulfils all the requirements. Amongst them main requirement is that the product must be safe. [1]

In-process control tests should be carried out before the manufacturing process is completed. The function of in-process quality controls is to monitor and if necessary, adaptation of the manufacturing process in order to comply with the specification. This may involve control of equipment and environment too.

In-process materials should be tested for their physical parameters and its quality attributes, which are later approved or rejected by the quality control department, it is depending on the results of the manufacturing process. Rejected In-process material ought to be distinguished and controlled under quarantine system, designed to prevent their user in manufacturing. Standard operating procedures should be established and followed that describe the in-process controls and tests. During the manufacturing process, certain tests are conducted where the acceptance criterion is identical to or smaller than the release requirement, (e.g., pH of solution) which may satisfy requirements when the test is included in the specification. [2]After the manufacturing process Finished Product Controls (FPC) are carried out. These tests are use to study

qualitative and quantitative characteristics along with test procedure and their acceptance limits, with which the finished product must comply throughout its valid shelf life. Specifications of the finished product, depends on the quality characteristics associated with the manufacturing process should be considered.During the time of development and during the time of validation of manufacturing process, an appropriate specification for each aspect of the quality studied should be determined. The objective of specifications is the aspects which are considered to be critical and should be verified routinely. Marketing authorization set the limits of specification of finished product at the time of batch release, such that the specifications proposed at the end of shelf life are guaranteed and are established on the basis of a critical detailed review of the data gathered from the batches analyzed. [3]

In the world, pharmacopoeias vary to different countries, such as Indian Pharmacopoeia (IP), British Pharmacopoeia (BP), United States Pharmacopoeia (USP), European Pharmacopoeia (PhEur), International Pharmacopoeia (PhInt) and Japanese Pharmacopoeia (JP). This study has been done to show the quality parameters for pharmaceutical tablets and capsules according to the pharmacopoeias that are part of in-process and finished products quality control tests.

OBJECTIVES OF IN-PROCESS QUALITY CONTROL

The objective of in-process quality control is to optimize the whole applied technological procedure. Another objective is to monitor control and improve effectively the whole applied operations at the every stage of the finished pharmaceutical products and also Quality control & Process Control, inspection of raw material, equipment, environment, process, testing with respect to specification, packing and so on. [4]

Universal tests for pharmaceutical tablet [5, 15, &16]

Approximately 50% dosage in market is tablet. For pharmaceutical tablet the universal tests are given below. These are four tests.

Description

This test includes description of tablet which is based on physical appearance of tablet. Such as tablet may be white, round, biconvex, film-coated tablet, imprinted with Rx on one side. It is a qualitative description.

Identification

This test is performed to check the activity of the pharmaceutical active ingredient (API) in the pharmaceutical tablet. This test should be able to identify the compounds which have closely related structure.

Assay

This test determines the strength or content of the API in the pharmaceutical tablet and it is also called a content test.

Impurities

This test determines the presence of any component that is not the API or excipients of pharmaceutical tablet. The process impurity is the most common type of impurities. That are arises from the new drug substance synthesis, degradation products of the API, or both.

Physical parameters of pharmaceutical tablets that are controlled by IPQC tests are temperature, pressure, moisture content, time, weight, particle size, hardness, loss on drying, disintegration time, color, compactness, integrity etc. FPQC test for pharmaceutical tablets are assay, uniformity of content, uniformity of mass, weight variation, friability test, content of active ingredients, hardness test, disintegration test, dissolution test etc.

IPQC and FPQC test for pharmaceutical tablets according to pharmacopoeias are listed below

In-process Quality control test for pharmaceutical tablet

Size and Shape

The size and shape of the tablet should be according to need of the dose requirement and can be dimensionally described monitored and controlled. It is determined by the tooling during the compression processes.

Color and Odor

For ease of identification many pharmaceutical tablets use color and it also helpful for consumer acceptance. But it must be uniform within a single tablet, from tablet to tablet and from batch to batch. Stability problem may be indicated by odour in batches of tablets e.g. vitamins have a characteristic odour. For the chewable tablet taste is importance factor for consumer acceptance.

Unique Identification Markings

Pharmaceutical companies often use some type of unique markings on tablets in addition to color, for rapid identification of their product these markings utilize some form of embossing, engraving or printing of the company name or symbol or a product code.

Moisture Content of Granules

Granules should possess sufficient strength to withstand normal handling and mixing processes without breaking down and producing large amounts of fine powder. On the other hand, some size reduction during compaction into tablets is desirable to expose the areas of clean surface necessary for optimum bonding to take place so moisture content is the very important factor for producing good pharmaceutical product.

Weight Variation Test

According to the USP this tablet is performed on 20 tablets by calculating the average weights and comparing with the individual tablet. The value of

weight variation test is expressed in percentage. Formula for weight variation test

Weight Variation = (Iw - Aw)/Aw X 100%

Where,

Iw = Individual weight of tablet

Aw = Average weight of tablet.

As per USP the tablet complies with the test if not more than 2 of the individual masses deviate from the average mass by more than the percentage deviation as shown in Table 1 and none deviates by more than twice that percentage.

Table1: limits for weight variation test as per IP, BP, USP [6, 7, 8]

Average mass (mg)		Percent Deviation (%)
IP/BP	USP	
80 mg or less	130mg or less	±10 %
More than 80mg or less than 250mg	130mg to 324 mg	±7.5%
250 mg or More	More than 324 mg or More	± 5%

Content uniformity test[6,7,8]

This test helps to ensure that the whether the content of tablet is properly mixed or not. Content uniformity test is performed randomly on 10 individual tablet.

IP: Active less than 10mg or 10%

BP: Active less than 2 mg or 2%

USP: Active less than 25mg or 25%

10 tablets limits NMT 1 tablet deviate 85 – 115% & none outside 75 – 125% of the average Value IP /BP/ USP (Relative standard deviation less than or equal to 6%)
If 2 or 3 individual values are outside the limits 85-115% of the average value, & none outside 75 – 125% repeat for 20 tablet
Complies when 30 tablets NMT 3 of the individual values are outside the limits 85 – 115% of the average values and none outside 75 – 125 %.

Thickness

The thickness of a tablet is the only dimensional variable related to the process, Thickness of tablets measured by a micrometer. Other techniques involve placing 5 or 10 tablets in a holding tray, where their total thickness may be measured by a sliding caliper scale. Thickness of tablet should be controlled within a ± 5 % variation of a standard. Thickness must be controlled to facilitate packaging. It is expressed in mm.

Hardness Test

For this test tablet hardness tester is use to check the hardness of the tablet. Monsanto, Pfizer Schleuniger these are the examples of hardness testers. Monsanto hardness tester consists of a barrel containing a compressible spring held between two plungers. The lower plunger is placed in contact with the tablet and zero reading is taken. The upper plunger is then forced against a spring by turning a threaded bolt until the tablet fractures. As the spring is compressed, a pointer rides along a gauge in the barrel to indicate the force. The force of fracture is recorded in kilogram. Ten tablets are crushed and measure their hardness and the allowable range is between 4 - 6 kg (40 - 60 N) unless otherwise specified. [9]

Friability Test

Friability of a tablet can determine in laboratory by Roche friabilator. For this test twenty tablets are weighed and placed in the friabilator and then operated at 25 rpm for 4 minutes. The tablets are then dedusted and weighed. The difference in the two weights is used to calculate friability and the value of friability is expressed in percentage. It is calculated by the following formula:

Friability = (Iw – Fw)/ Iw x 100%

Where,

Iw = Total Initial weight of tablets

Fw = Total final weight of tablets.

As stated by USP, if conventional compressed tablets that loss less than 0.5 % to 1 % (after 100 revolutions) of their weight are generally considered acceptable.

Rotation: 25 rpm or 100 Rotation in 4 min. [6]

Disintegration Test:

The USP disintegration apparatus consist of 6 glass tubes that are 3 inches long, open at the top, and held against a 10-mesh screen at the bottom end of the basket rack assembly. To test for disintegration time, one tablet is placed in each tube and the basket rack is positioned in specified medium at 37 ± 2 °C such that tablet remains 2.5 cm below the surface of the liquid on their upward movement and descend not closer than 2.5 cm from the bottom of the beaker. A standard motor driven device is used to move the basket assembly containing the tablets up and down through distance of 5 to 6 cm at a frequency of 28 to 32 cycles per minute. Perforated plastic discs may also be used in the test. These are placed on the top of tablets and impart an abrasive action to the tablets. The discs are useful for tablets that float. Operate the apparatus for the specified time (15 minutes for uncoated tablet unless otherwise justified and authorized. [6]

The tablet complies with the test, if the tablets disintegrate, and all particles pass through the 10-mesh screen in the time specified. If any residue remains, it must have a soft mass with no palpably firm core. The tablet complies with the test according to USP, if all of the tablets have disintegrated completely. If 1 or 2 tablets fail to disintegrate completely, repeat the test on 12

additional tablets. The requirement is met if not less than 16 of the total of 18 tablets tested are disintegrated. The BP and IP limits for disintegration times of tablets are given in Table 2. [7]

Table 2: Limits for disintegration times of tablets as per IP, BP, USP [6, 7]

Categories of tablets	Disintegration time (min)		
	IP (min)	BP (min)	USP
Uncoated tablets	15	15	5-30 min.
Coated tablets	60	60	1 – 2 hrs.
Enteric-coated tablets	60	-	1 hr or as per individual monograph
Film-coated tablets	30	-	30 min or as per individual monograph
Effervescent tablets	5	5	Less than 3 min or as per individual monograph
Soluble tablets	3	3	-
Dispersible tablets	3	3	Less than 3 min or as per individual monograph
Orodispersible tablets	-	3	-
Gastro-resistant tablets	-	60	-
Oral lyophilisates	-	3	-

Dissolution Test

The BP or USP dissolution apparatus (Basket apparatus) consist of a cylindrical vessel with a hemispherical bottom, which may be covered, made of glass or other inert, transparent material; a motor; a metallic drive shaft; and a cylindrical basket. The vessel is partially immersed in a suitable water bath of any convenient size or heated by a suitable device such as a heating jacket. The water bath or heating device permits holding the temperature inside the vessel at 37 ± 0.5 °C during the test and keeping the bath fluid in constant, smooth motion. [6, 7, 18, 19]

For this test according to BP and PhEur place the stated volume of the dissolution medium (± 1 %) in the vessel of the specified apparatus. Assemble the apparatus; equilibrate the dissolution medium to 37 ± 0.5 °C and place 1 tablet in the apparatus, take care to exclude air bubbles from the surface of the tablet. Operate the apparatus at the specified rate. Within the time interval specified, or at each of the times stated, withdraw a specimen from a zone midway between the surface of the dissolution medium and the top of the rotating basket or blade, not less than 1 cm from the vessel wall. Where multiple sampling times are specified, replace the aliquots withdrawn for analysis with equal volumes of fresh dissolution medium at 37 °C or, where it can be shown that replacement of the medium is not necessary, correct for the volume change in the calculation. Keep the vessel covered for the duration of the test and verify the temperature of the medium at suitable times.

Perform the analysis using a suitable assay method as directed in the individual monograph. Repeat the test with additional tablets. Unless otherwise specified in the individual monograph, according to BP, USP, PhEur, JP and PhInt the requirements are met if the quantities of active ingredient dissolved from the tablets tested conform to the following acceptance criteria (Table 3).

Table 3: BP, USP, PhEur, JP and PhInt acceptance criteria for dissolution test of tablet [6, 7, 8, 10, and 11]

Stage	No. of tablet tested	Acceptance criteria
S1	6	Each unit is not Q + 5 %
S2	6	Average of 12 units (S1+ S2) is equal to or greater than Q, and no unit is less than Q-15%
S3	12	Average of 24 units (S1+ S2+ S3) is equal to or greater than Q, not more than 2 units are less than Q-15% and no unit is less than Q-25%

Universal tests for pharmaceutical Capsule [12]

10% market has acquired in the capsule dosage form. General tests for pharmaceutical capsule are as follows.

Description

This test includes description of capsule which is based on physical appearance of capsule. Such as capsule may be white cap, red body, imprinted with Rx on one cap. It is a qualitative description.

Identification

This test identifies the API in the pharmaceutical capsule. This test should be able to identify the compounds of closely related structure that are likely to be present.

Assay

This test determines the strength or content of the API in the pharmaceutical capsule and is sometimes called a content test.

Impurities

This test determines the presence of any component that is not the API or excipients of pharmaceutical tablet. The process impurities is the most common

type of impurities. That are arises from the new drug substance synthesis, degradation products of the API, or both.

B] IPQC AND FPQC TESTS

Appearance

Appearance of capsule must be uniform. For detect of any flaws in the integrity and appearance of the capsule, visual or electronic inspection should be undertaken. Evidence of physical instability is demonstrated by gross changes in appearance, including hardening or softening, cracking, swelling, mottling, printing mistake or discoloration of the shell. Defective capsules should be rejected.

Size and Shape

Hard capsules are made in a range of sizes, the standard industrial range of size for capsule is from 000 (the largest, 1.40 ml) to 5 (the smallest, 0.13 ml) are commercially available. Soft gel capsules are available in variety of shapes such as spherical (0.05–5 ml), ovoid (0.05–7 ml), cylindrical (0.15–25 ml), tubes (0.5–0 ml), pear (0.3–5 ml) etc.

Unique Identification Markings

Capsule surfaces may bear symbols or other unique identification markings for better identification.

Assay

In a capsule an active ingredient is present which is called API. So to prepare the capsule assay has to be done by using suitable analytical method to produce good finished product.

Content of Active Ingredients

For this test a sample of the contents is assayed as described in individual monographs and calculates the amount of active ingredient in each capsule. According to IP the range for the content of active ingredient stated in the monograph is based on the requirement that 20 capsules, or such other number as may be indicated in the monograph, are used in the assay. In the circumstances where 20 capsules cannot be obtained, a smaller number, which must not be less than 5, may be used, but to allow for sampling errors the tolerances are widened in accordance with Table 4. [6]

Table 4: IP limits for content of active ingredients [6]

Weight of active ingredients in each capsule (g)	Subtract from lower limit for sample of			Add to upper limit for sample of		
	15	10	5	15	10	5
0.12 or less	0.2	0.7	1.5	1.5	0.8	1.8
More than 0.12 Bust less than 0.3	0.2	0.5	1.2	0.3	0.6	1.5
0.3 or more	0.1	0.2	0.8	0.2	0.4	1.0

Content Uniformity Test[6, 7, 8, 10]

For this test according to BP determine the content of the active ingredient in each of 10 capsules (hard or soft) taken at random using the method given in the monograph or by any other suitable analytical method of equivalent accuracy and precision. Calculate the acceptance value (AV) using the following formula:

$$|M - X| + KS$$

Where,

M = Reference value.

X = Mean of individual content (x1, x2..... xn) expressed as percentage of the label claim.

K = Acceptability constant.

S = Sample standard deviation

As per BP, capsules comply with the test if not more than one of the individual values thus obtained is outside the limits 85 to 115 percent of the average value and none is outside the limits 75 to 125 percent. The capsules fails to comply with the test if more than 3 individual contents are outside the limits of 85 percent to 115 percent of the average content or if one or more individual contents are outside the limits of 75 percent to 125 percent of the average content. If 2 or 3 individual values are outside the limits 85 to 115 percent of the average values, repeat the determination using another 20 capsules. The capsules comply with the test if in the total sample of 30 capsules not more than 3 individual values are outside the limits 85 to 115 percent and none is outside the limits 75 to 125 percent of the average value.

As stated by IP, BP, USP and PhEur limits for content uniformity (CU) and mass variation (MV) tests of capsules are given in Table 5. , According to IP , this test is not applicable for capsules containing multivitamins and trace elements.

Mass Variation Test [6, 7, 8]

For hard capsules according to BP accurately weigh 10 capsules individually, taking care to preserve the identity of each capsule. Remove the contents of each capsule by suitable means. Accurately weigh the emptied shells individually, and calculate for each capsule the net mass of its contents by subtracting the mass of the shell from the respective gross mass. Calculate the active substance content in each capsule from the mass of product removed from the individual capsules and the result of the

assay. Calculate the AV using the following formula:

Xi = Wi × A/W

Where,

x1, x2,..., xn = Individual estimated contents of the dosage units tested.

w1, w2... wn = Individual masses of the dosage units tested.

A = Content of active substance (percentage of label claim) obtained using an appropriate analytical method (assay).

W = Mean of individual weights (w1, w2... wn).

For soft capsules consistent with BP accurately weigh 10 intact capsules individually to obtain their gross masses, taking care to preserve the identity of each capsule. Then cut open the capsules by means of a suitable clean, dry cutting instrument such as scissors or a sharp open blade, and remove the contents by washing with a suitable solvent. Allow the occluded solvent to evaporate from the shells at room temperature over a period of about 30 min, taking precautions to avoid uptake or loss of moisture. Weigh the individual shells, and calculate the net contents. Calculate the active substance content in each capsule from the mass of product removed from the individual capsules and the result of the assay. Calculate the AV using the formula given above.

According to BP and USP, the requirement is met if the acceptance value of 10 capsules is less than or equal to 15 percent. If acceptance value is greater than 15 percent, test the next 20 capsule and calculate, the acceptance value. The requirements are met if the final acceptance value of the 30 capsule is less than or equal to 15 percent and no individual content of the capsule is less than (1 – 25 × 0.01) M or more than (1 + 25 × 0.01) M in calculation of acceptance value under mass variation or content uniformity.

Table 5: IP, BP, USP and PhEur limits for content uniformity (CU) and mass variation (MV) [6, 7, 8, 10]

Capsule	Dose and ratio of active substance	
	25 mg or 25> %	< 25 mg or < 25 %
Hard	MV	CU
Soft	CU	CU

Uniformity of Mass (Weight) [7, 8, 10, 11]

For this test weigh an intact capsule. Open the capsule without losing any part of the shell and remove the contents as completely as possible. To remove the contents of a soft capsule, the shell may be washed with ether or other suitable solvent and the shell allowed to stand until the odor of the solvent is no longer perceptible. Weigh the shell. The weight of the contents is the difference between the weighing. Repeat the procedure with a further 19 capsules. Determine the average mass.

According to IP, BP, PhEur and PhInt capsules not more than 2 of the individual masses deviate from the average mass by more than the percentage deviation shown in the Table 6 and Table 7 respectively and none deviates by more than twice that percentage.

Table 6: IP, BP, and PhEur limits for uniformity of mass (weight)

Average mass (mg)	Percentage Deviation (%)
Less than 300	10
300 or more	7.5

Table 7: PhInt limits for uniformity of mass (weight)

Net mass	Percentage deviation (%)	Number of capsule
Less than 300	10	Minimum 18
	20	Maximum 2
300 or more	7.5	Minimum 18
	15	Maximum 2

Disintegration Test

USP disintegration test:

The USP disintegration apparatus consist of 6 glass tubes that are 3 inches long, open at the top, and held against a 10-mesh screen at the bottom end of the basket rack assembly. To test for disintegration time, one capsule is placed in each tube and the basket rack is positioned in specified medium at 37±2ºC such that capsule remains 2.5 cm below the surface of the liquid on their upward movement and descend not closer than 2.5 cm from the bottom of the beaker.

A standard motor driven device is used to move the basket assembly containing the capsules up and down through distance of 5 to 6 cm at a frequency of 28 to 32 cycles per minute. Perforated plastic discs may also be used in the test. These are placed on the top of capsules and impart an abrasive action to the capsules. The discs are useful for capsules that float. Operate the apparatus for the specified time. The capsule complies with the test, if the capsules disintegrate, and all particles pass through the 10-mesh screen in the time specified. If any residue remains, it must have a soft mass with no palpably firm core. [21]

The capsule complies with the test according to USP, if all of the capsules have disintegrated completely. If 1 or 2 capsules fail to disintegrate completely, repeat the test on 12 additional capsules.

The requirement is met if not less than 16 capsule of the total of 18 capsules tested are disintegrated.

IP BP and USP disintegration test:

According to IP,BP and USP the disintegration time of various capsules is given in Table 8.

Table 8: Disintegration time for various capsules according to USP, IP, and BP [6, 7, 8]

Capsule	Disintegration time (min)	
	IP	BP
Hard capsule	30	30
Soft capsule	60	30
Enteric capsule	60	-
Gastro resistant capsule	-	60
Vaginal capsule	-	30
Rectal capsule	-	30

According to IP, the disintegration test is not applicable to modified-release capsules. For those hard or soft capsules for which a requirement for dissolution is included in the individual monograph, the requirement for disintegration does not apply. As said by BP apparatus, A is used for capsules that are not greater than 18 mm long and for larger capsules apparatus B is used.

Dissolution Test

The BP or USP dissolution apparatus (Basket apparatus) consist of a cylindrical vessel with a hemispherical bottom, which may be covered, made of glass or other inert, transparent material; a motor ; a metallic drive shaft; and a cylindrical basket. The vessel is partially immersed in a suitable water bath of any convenient size or heated by a suitable device such as a heating jacket. The water bath or heating device permits holding the temperature inside the vessel at 37±0.5°C during the test and keeping the bath fluid in constant, smooth motion. [6, 8, 20]

For this test as per BP and PhEur place the stated volume of the dissolution medium (±1 %) in the vessel of the specified apparatus. Assemble the apparatus; equilibrate the dissolution medium to 37±0.5°C. Place 1 capsules in the apparatus, taking care to exclude air bubbles from the surface of the capsules. Operate the apparatus at the specified rate. Within the time interval specified, or at each of the times stated, withdraw a specimen from a zone midway between the surface of the dissolution medium and the top of the rotating basket or blade, not less than 1 cm from the vessel wall. [7, 10]

Where multiple sampling times are specified, replace the aliquots withdrawn for analysis with equal volumes of fresh dissolution medium at 37°C or, where it can be shown that replacement of the medium is not necessary, correct for the volume change in the calculation Keep the vessel covered for the duration of the test and verify the temperature of the medium at suitable times.

Perform the analysis using a suitable assay method as directed in the individual monograph. Repeat the test with additional capsules. According to BP, USP, PhEur, PhInt and JP unless otherwise specified in the individual monograph, the requirements are met if the quantities of active ingredient dissolved from the capsules tested conform to the following acceptance criteria as shown in Table 9.

Continue testing through the 3 stages unless the results conform at either S1 or S2. The quantity Q, is the specified amount of dissolved active substance, expressed as a percentage of the labelled content; the 5 percent, 15 percent, and 25 percent values in the capsule are percentages of the labelled content so that these values and Q are in the same terms.

Table 9: BP, USP, PhEur, PhInt and JP acceptance criteria for dissolution test of capsule [7, 8, 10, & 12]

Stage	No. of capsule tested	Acceptance criteria
S1	6	Each unit is not less than Q =5%
S2	6	Average of 12 units (S1+S2) is equal to or greater than Q, and unit is less than Q -15%
S3	12	Average 24 units (S+S+S) is equal to or greater than Q, not less than 2 and no unit are lessQ-15 % and no unit is less than -25

Moisture Permeation Test[6, 12, 13]

The USP requires determination of the moisture permeation characteristics of single-unit and unit dose containers to ensure their suitability for packaging capsules. The degree and rate of moisture penetration are determined by packaging the dosage unit together with a color revealing desiccant pellet, exposing the packaged unit to known relative humidity over a specified time, observing the desiccant pellet for color change. Any change in color indicates absorption of moisture. By measuring pre-test weight and protest weight of pellet, amount can be calculated.

Stability Test[12, 13, 17]

The capsule manufacturers routinely conduct accelerated physical stability tests on all new capsule products as an integral part of the product development program. The following tests have proved adequate for determining the effect of the capsule shell content on the gelatine shell. The tests are strictly relevant to the integrity of the gelatine shell and should not be confused as stability tests for the active ingredients in the capsule content.

The results of such tests are used as a guide for the preformulation of the capsule content or the capsule shell, or for the selection of the proper retail package. The test conditions for such accelerated stability tests are shown in above, Table.10.The capsules at these stations are observed periodically for 2 weeks. Both gross and subtle effects of the storage conditions on the capsule shell are noted and recorded. The control capsule should not be affected except at the 80 percent RH (relative humidity) station, where the capsule would react as described under the effects of high humidity.

Table 10: Test conditions for accelerated stability tests for capsule dosage forms [13, 14, & 20]

Test conditions	Observation
80% RH at room temperature in an open container.	Capsule are observation periodically for 2 weeks, both gross and subtle effects of the storage condition are noted and recorded. The control capsule should not be affected except at the 80% RH station
40 ^{0}C in an open container	
40 ^{0}C in a closed container (glass bottle with tight screw-cap)	Except at the 80% RH stations

CONCLUSION:

In-process quality control tests are designed to provide early warning for quality or problems arising during production. These in-process controls are necessary to ensure the quality of the product. From the review , it can be concluded that there is slight difference in, In-process quality control tests of Indian pharmacopoeia; British pharmacopoeia and united state pharmacopoeia. Some of the tests are not available in some pharmacopoeia. The product must be formulated according to the requirements listed in corresponding pharmacopoeia. Different pharmacopoeia sets different limits for IPQC tests Nevertheless; the main purpose of all pharmacopoeias is to produce good quality pharmaceutical for human health.

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