2022/2023

Fifth Stage

First Semester/ Industrial Pharmacy II

Soft gelatin capsules

Lecture 19

29/12/2022

Dr. Ahmed Najim Abood

Assistant Professor in Pharmaceutics

ahmed.abood@uobasrah.edu.iq

Soft-gels

- ✓ Completely sealed DF, more flexible capsules .
- ✓ Their sizes are estimated in volume units (minims).
- ✓ Found into different shapes (round, oval, oblong and tube).
- ✓ Are manufactured in one process and machine.

Advantages and disadvantages

They are more suitable for oily API regarding the taste and solubility.
But there is more manufacturing difficulty, stability problems

Can be subdivided into several types like:

1) Melt-able = similar to suppositories
2) Chewable = similar to chewable tablets
3) Suck-able = similar to lozenges
4) Seamless round = specific method
5) Controlled released softgels = similar to modified released tablets
6) Enteric coated softgels = similar to enteric coated tablets

Manufacturing of soft-gels

Materials of the capsule shell are gelatin (type B is commonly used??), plasticizer, water, preservative ?? , colorant, opacifier and others (flavors, sweetener, release modifier)

Plasticizers or softeners give the elastic properties, like glycerol , sorbitol, or mixture ?? of them in concentrations (20-30%), more than 30% give too flexible and tacky property, while less than 20% give too brittle property.

Other ex. maltitol and PEG

Water used as solvent, and can give flexibility, its amount at first is (0.7-1 part to each part of gelatin) and then with drying is reduced to (13-16%), over drying may cause brittleness.

Titanium dioxide (a colorant and/or opacifier) is used for visual appeal and/or reducing of light effect.

In soft gelatin capsule the amount of plasticizer used is more and used to reduce Tg of gelatin shell and/or promotes the retention of moisture.

In soft gelatin capsule the plasticizer and gelatin ratio is 0.8 : 1

In hard gelatin capsule the plasticizer and gelatin ratio is 0.4 : 1

Capsule fills are:

1) Non aqueous liquids like vegetable oils (ex. Soybean oil) and fatty acid esters, with co-solvent or SAA.
2) Suspension (with viscosity enhancer and SAA)
3) Pasty materials
4) Preconcentrate of a self emulsifying or self-microemulsifying system
5) water miscible liquids like PEG 400,600, Tweens, Pluronics , with co solvent, SAA and viscosity enhancer.

This fill must be:

1) No interacted with gelatin.
2) Non moisture sensitive.
3) Non thermo-sensitive.
4) Neither extreme acidic nor extreme basic (pH in range of 2.5-9) to avoid hydrolysis or tanning of gelatin.

Non-gelatin softgels

Vegicaps® are animal-free, made of seaweed extract and gluten-free starch. HPMC capsules are preferred for water sensitive drugs.

Soft gels production

We have several processes:

1) Plate process (old method)
2) Rotary die process
3) Reciprocating process
4) Accogel process (Stern machine): similar to rotary die process, but used for solid fill.
5) Bubble method: used for seamless type

In these processes: manufacturing of the shell, preparation of fill, filling and sealing occurred in one process.

Sealing may be preformed under effect of heat (about 40◦C) or pressure.

The fills must be homogeneous and air free.

Rotary die process:

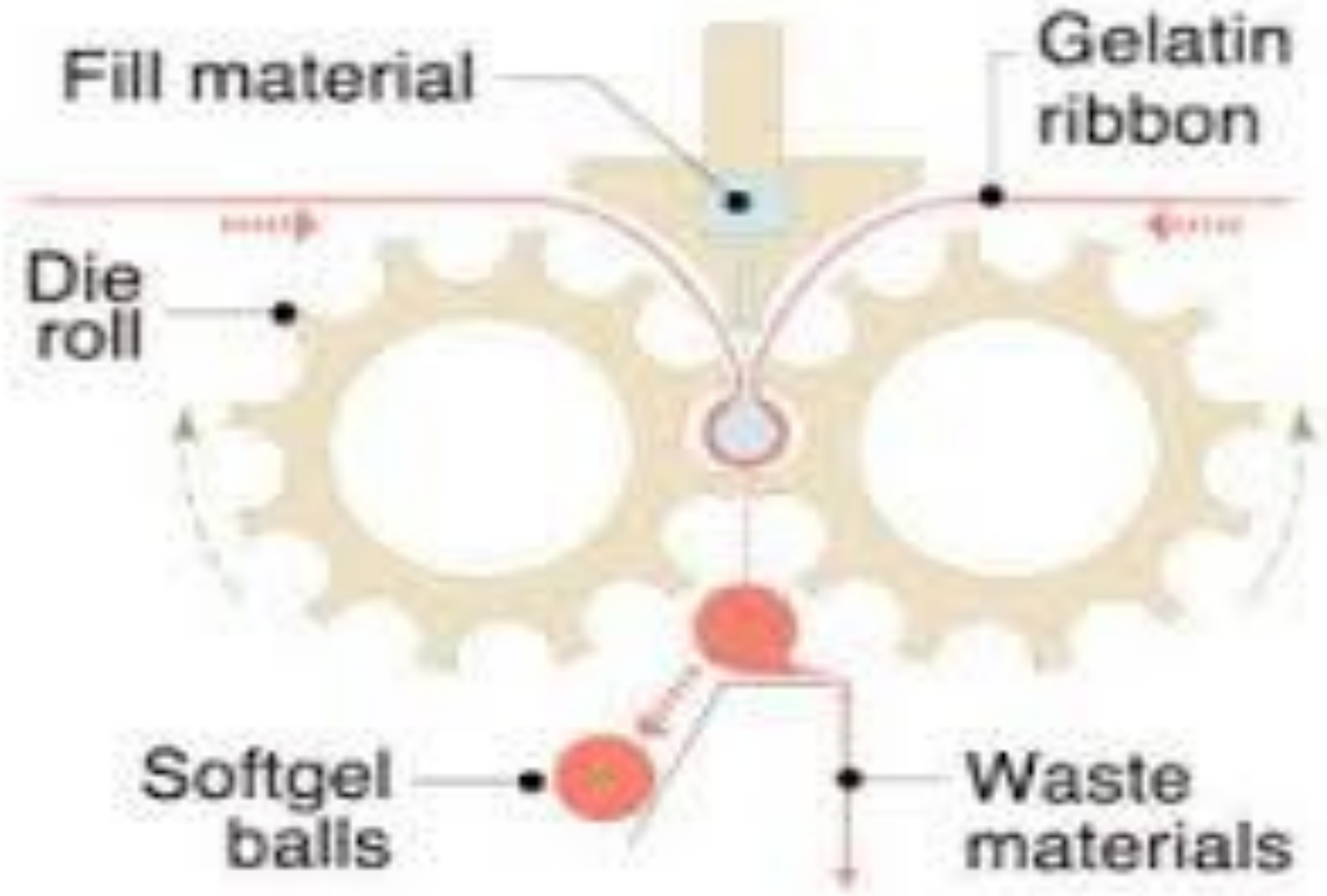
More efficient and productive, gelatin shells formed by die rolls in form of ribbons.

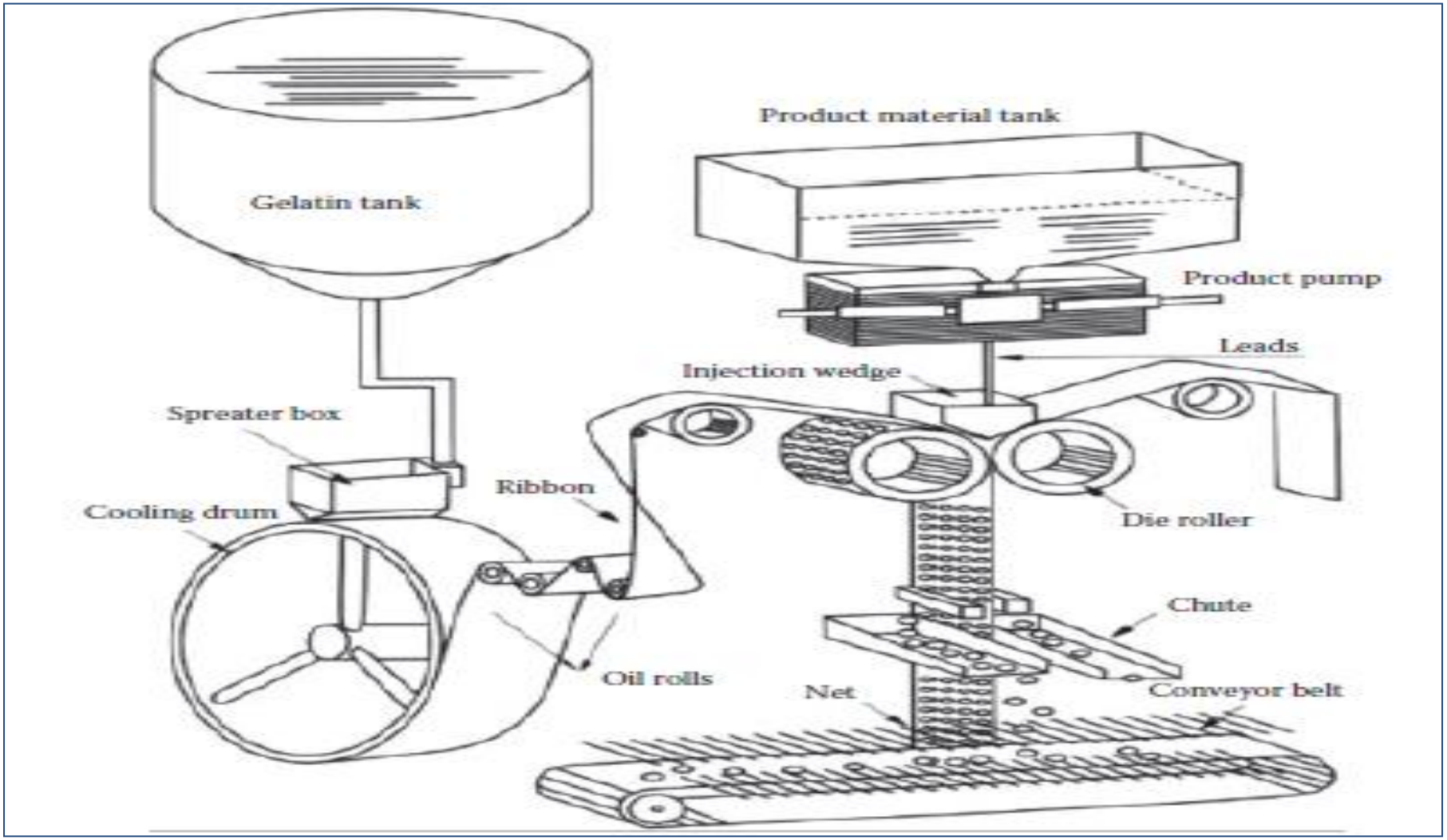
The material to be encapsulated flows by gravity.

The gelatin sheets are feed on rolls contain small orifice lined up with the die pocket of the die roll.

Two plasticized gelatin ribbons are continuously and simultaneously fed with the liquid or paste fill between the rollers where the capsule are simultaneously filled, shaped, hermetically sealed and cut from the gelatin ribbon.

The sealing of the capsule is achieved by mechanical pressure on the die rolls and the heating (37-40ºC) of the ribbons by the wedge.

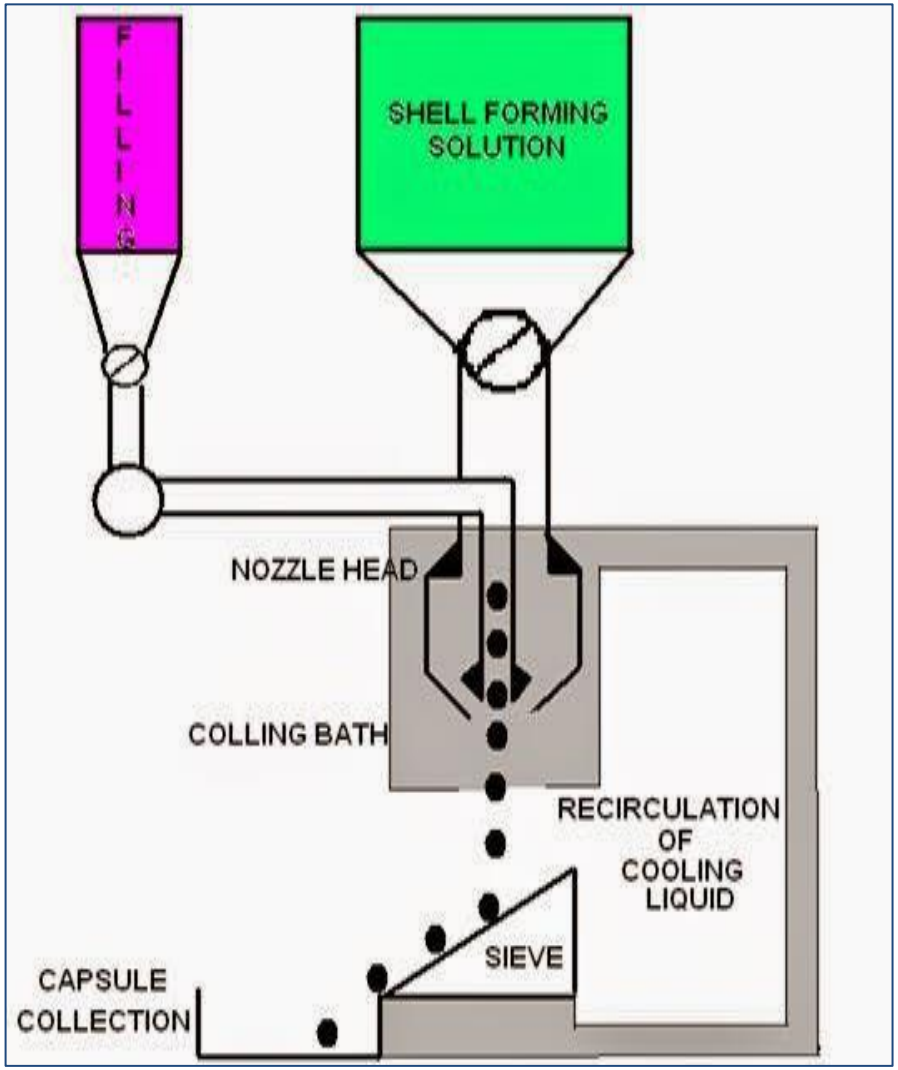

Fill material
Gelatin ribbon
Die roll
Softgel balls
Waste materials


Product material tank
Gelatin tank
Product pump
Leads
Injection wedge
Spreater box
Ribbon
Cooling drum
Die roller
Chute
Oil rolls
Net
Conveyor belt

Bubble or Globex Method

Soft capsules are collected, washed with organic solvent to remove residues of cooling liquid (liquid paraffin), and gently dried at a relative humidity of 20% in infrared tunnels.

Advantage: production of seamless capsules which are tamper-evident and free of contamination or entrapped air.



Stability of softgels

- The softgel shell is considered as a good barrier against the diffusion of oxygen from the environment into the liquid content of the product, the effecting factors are summarized into the following equation:

$$q = \frac{PAt\ (p1-p2)}{h}$$

q= quantity of oxygen

P= Permeation corfficient A= area t= time of diffusion

p1-p2 = partial pressure difference h= thickness

19

Extreme temperature and humidity can affect the mechanical properties of softgels, by affecting the residual water content.

Evaluation of capsules

1) In processing tests:(Mostly non official)

a- Gelatin shell tests (size, thickness, color, leakage test, MC and mechanical properties)

b- Content fill tests : solubility, homogeneity, flowability, particle size distribution, density and air entrapment.

2) After processing tests: (Official test)

a- Disintegration test

b- Weight variation

c-Content uniformity test (As in tablets)

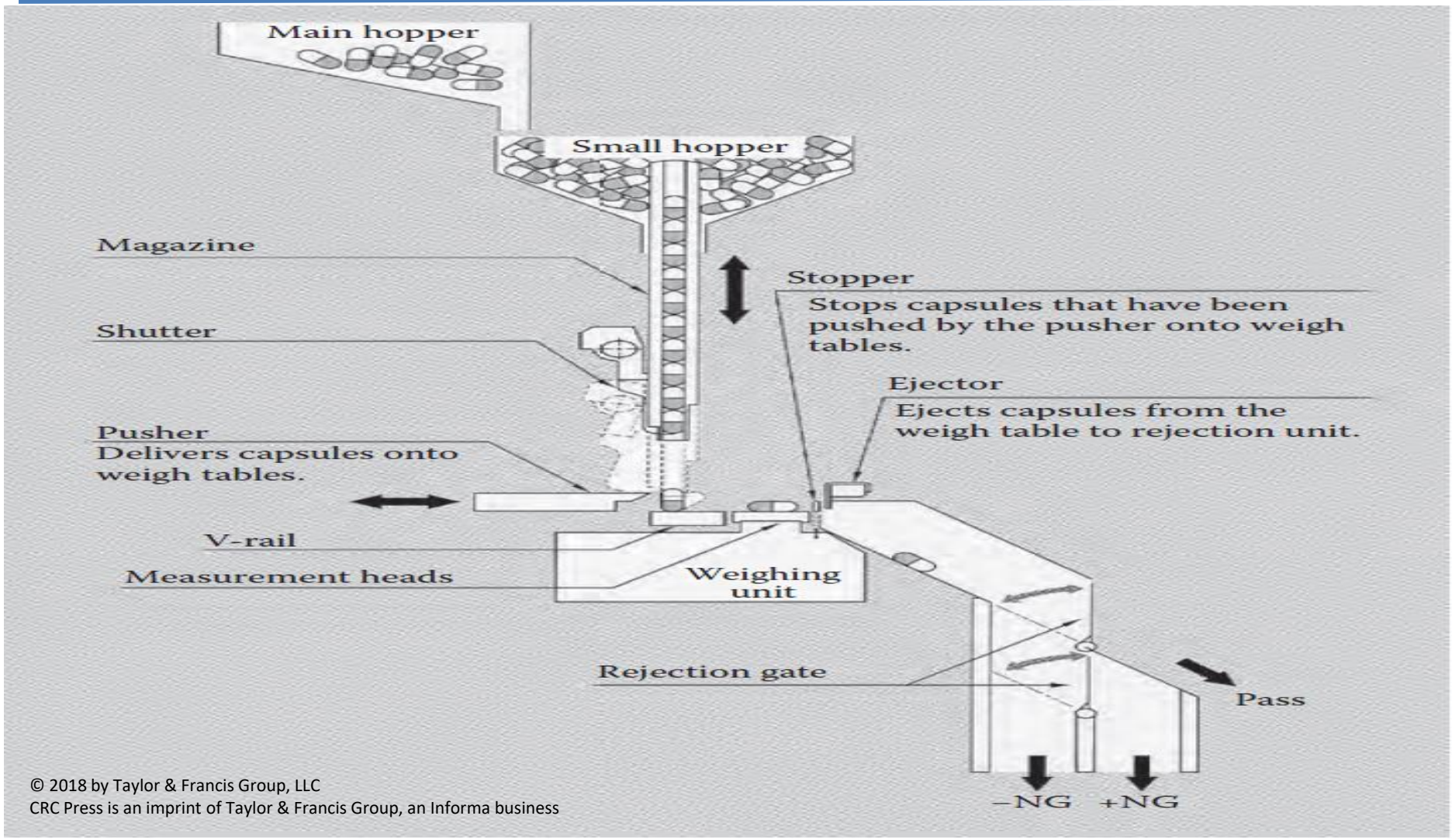
d- Dissolution test (generally as in tablets)

e- Moisture permeation test

f- Moisture content

h- Microbial content

g- Stability test



Moisture Permeation Test

The USP requires determination of the moisture permeation properties 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 RH over a specified time, observing the desiccant pellet for color change (indicating the absorption of moisture), and comparing the pretest and posttest weight of the packaged unit.