تقم كلية الصيدلة / جامعة بغداد
وحدة الشؤون العلمية الورشة الموسومة

In Situ Gel Oral Spray

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Gel-forming Spray

- Sprayable in situ gel is an innovative delivery device that allows the application of liquid in a sprayable form that undergoes phase transition under physiological conditions.

Advantages

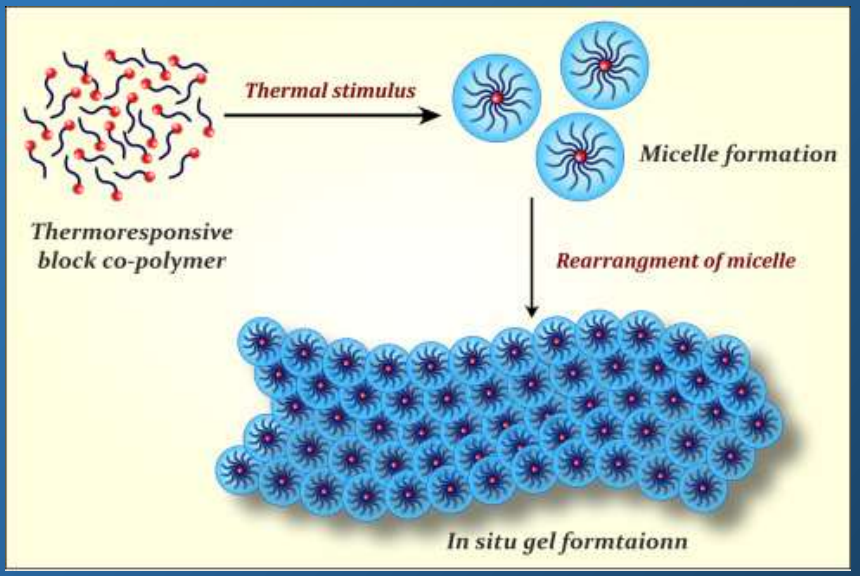
1. Sprayable gels may also be created with **bio-adhesive properties** to aid in **drug targeting**.
2. Sprayable gel's "Sol-Gel" transition aids in the **regulated and prolonged release** of the medicines.
3. **Ease of application**, and it is possible to provide medication to patients who are unconscious.
4. Improved **patient compliance**

Disadvantages

1. **Stability issues** , drug is more prone to deterioration in its sol form.
2. **Eating and drinking may be restricted** for a short period of time after taking the medicine.
3. **Difficulty resistance to strong mechanical movement** could cause the spray gel to dissolve too soon or to flow away from the intended local s pot.
4. Only medicines with a **low dosage requirement** may be administered.

Gelation Mechanisms

1



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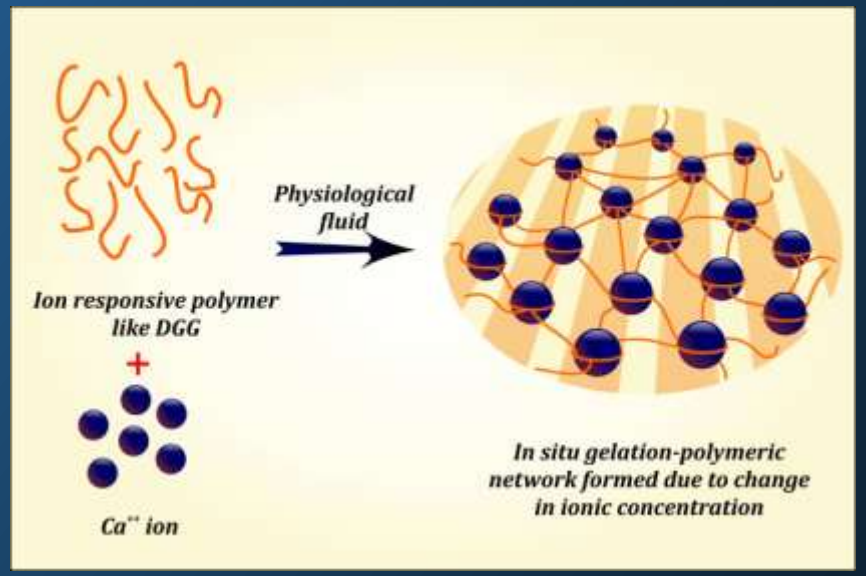

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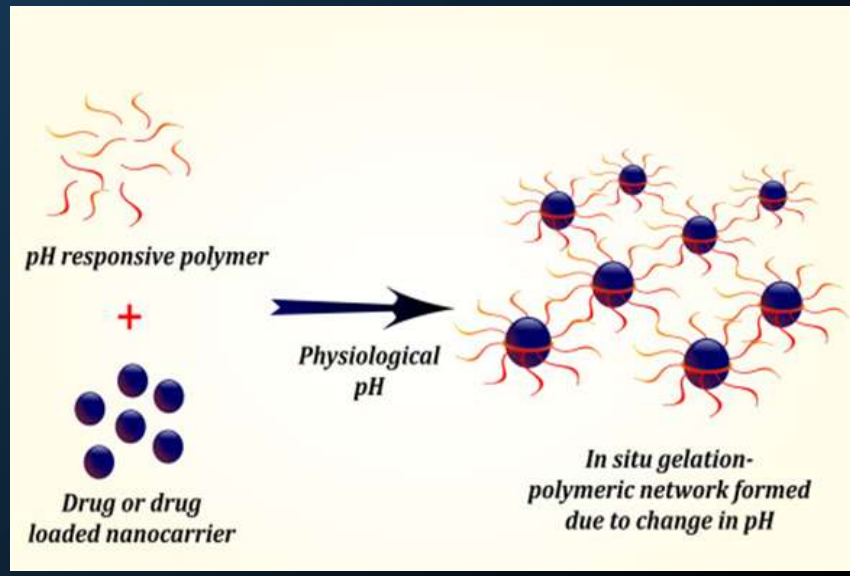
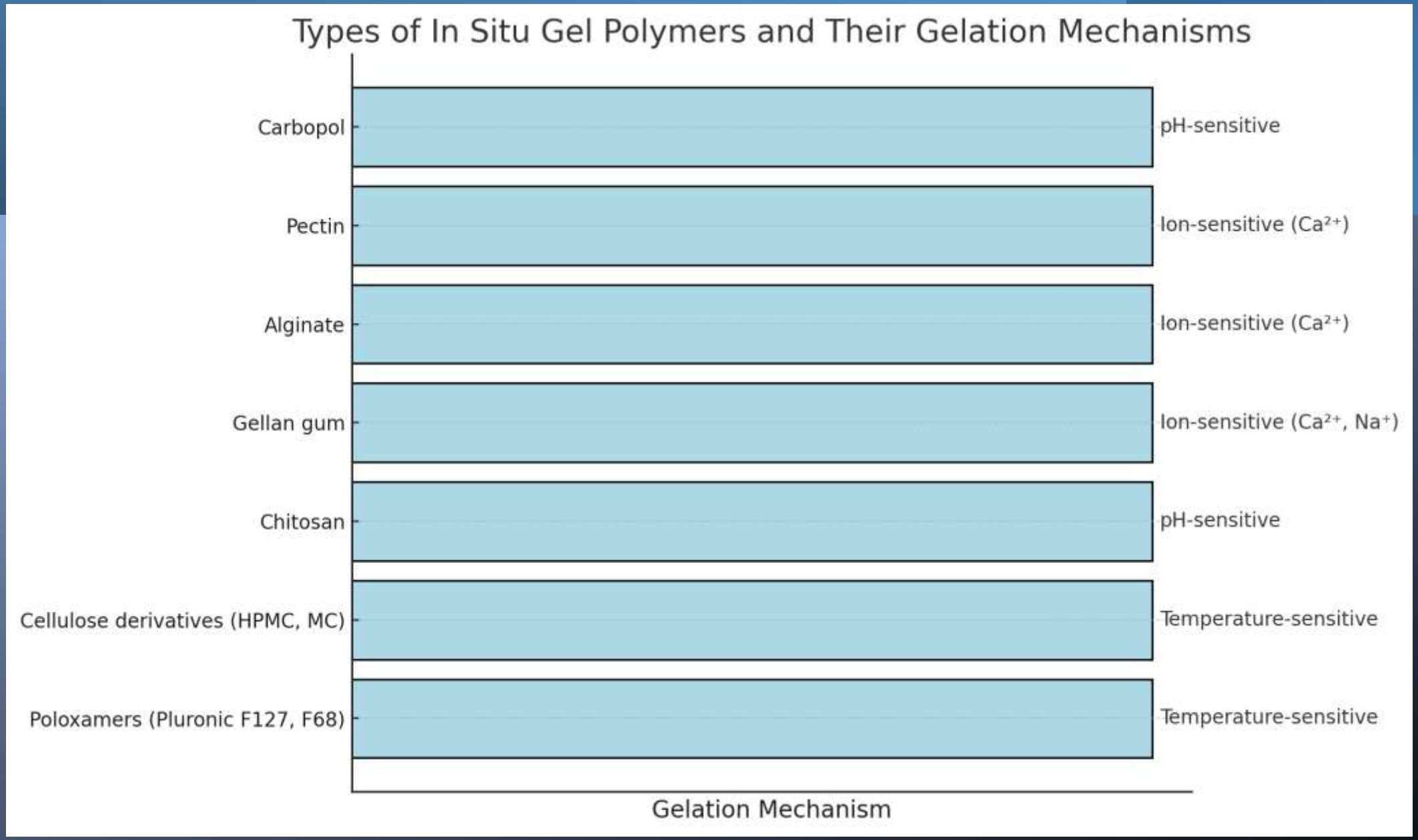
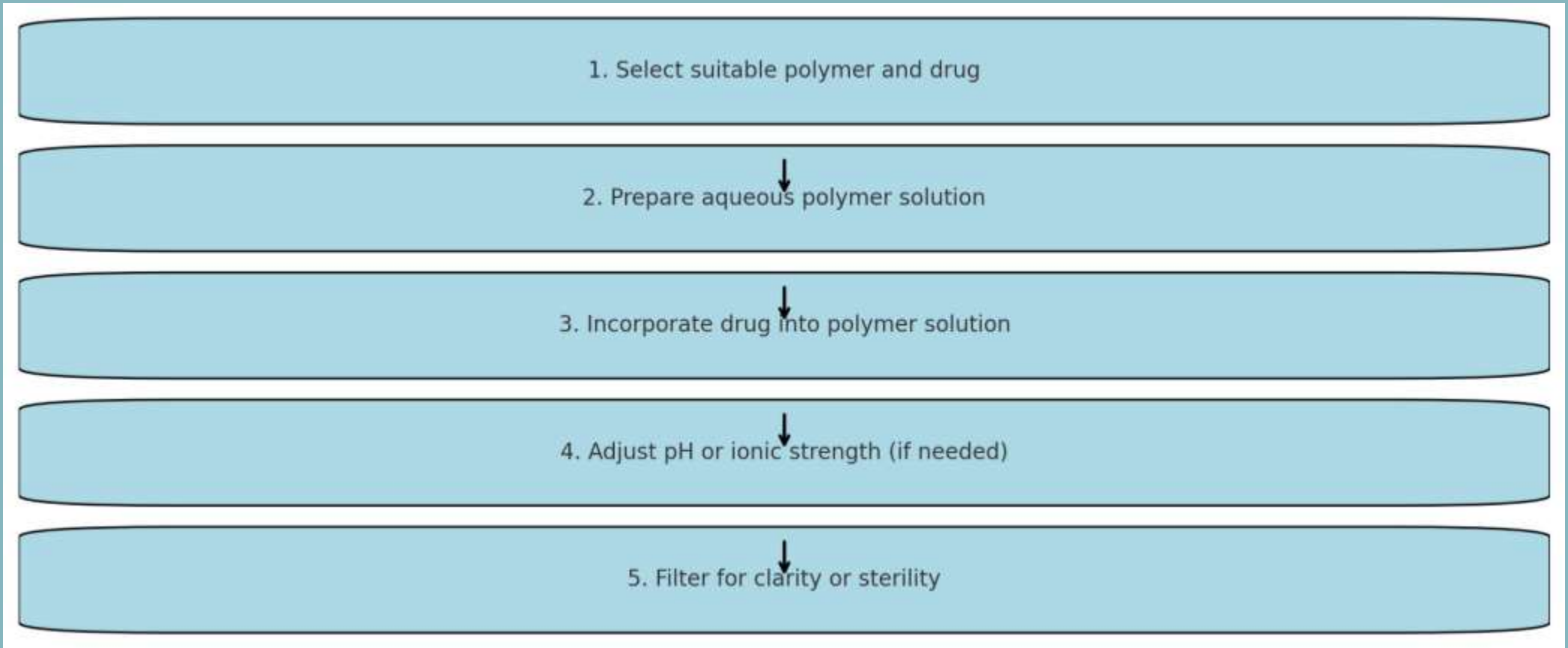



Types of In Situ Gel Polymers and Their Gelation Mechanisms
Carbopol
Pectin
Alginate
Gellan gum
Chitosan
Cellulose derivatives (HPMC, MC)
Poloxamers (Pluronic F127, F68)
pH-sensitive
Ion-sensitive (Ca²⁺)
Ion-sensitive (Ca²⁺)
Ion-sensitive (Ca²⁺, Na⁺)
pH-sensitive
Temperature-sensitive
Temperature-sensitive
Gelation Mechanism



General Steps of ING Preparation

In Situ Gels Evaluation

1. **physical evaluations:**
   a) Appearance (Preferably, the gels should be transparent),
   b) Clarity (using a black and white background),
   c) Homogeneity (optical observation of particle roughness under the light).

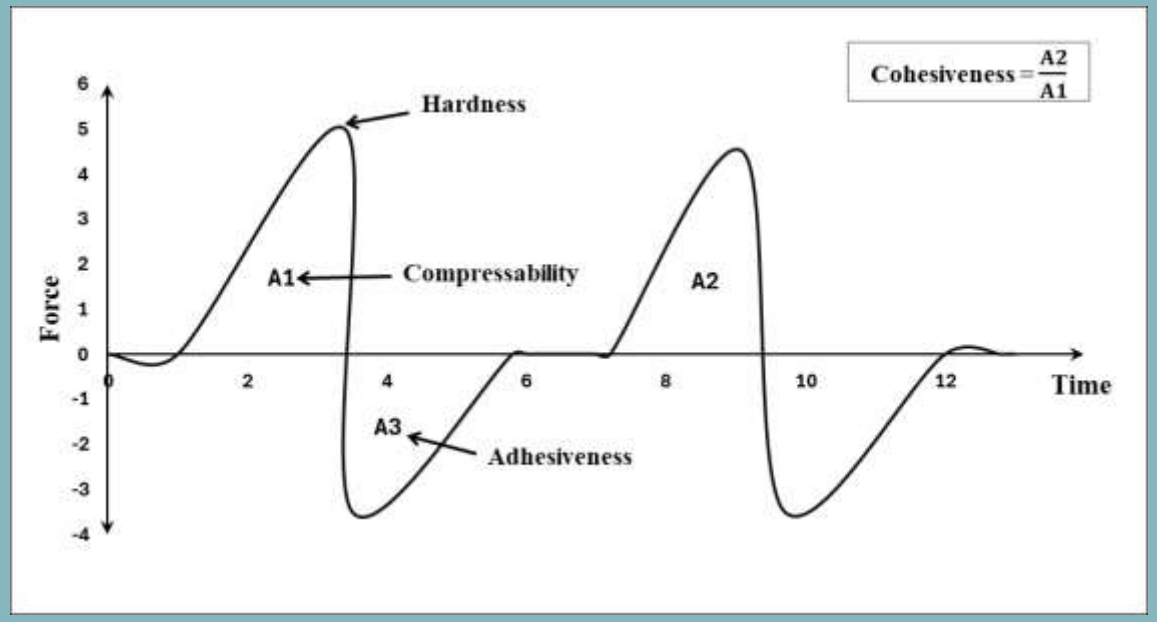
2. **Sol-gel transition temperature**
   a) Tube Inversion Method (Visual Observation)
   b) Rheological Analysis (Viscosity/Elasticity Measurements).
   c) Differential Scanning Calorimetry (DSC)
   d) Falling Ball Method (or Magnetic stirrer method)

3. **Gelling time**

4. **pH**

In Situ Gels Evaluation

6. **Spreadability:** represents the ease of formula application.
7. **Viscosity Study:** Before and after the gelation process, in situ gel preparations should exhibit pseudo-plastic and Newtonian flow. It should be < 1000 m Pas ('sol') to allow application using spray before gelling.
8. **Texture profile analysis (TPA):** mechanical properties.

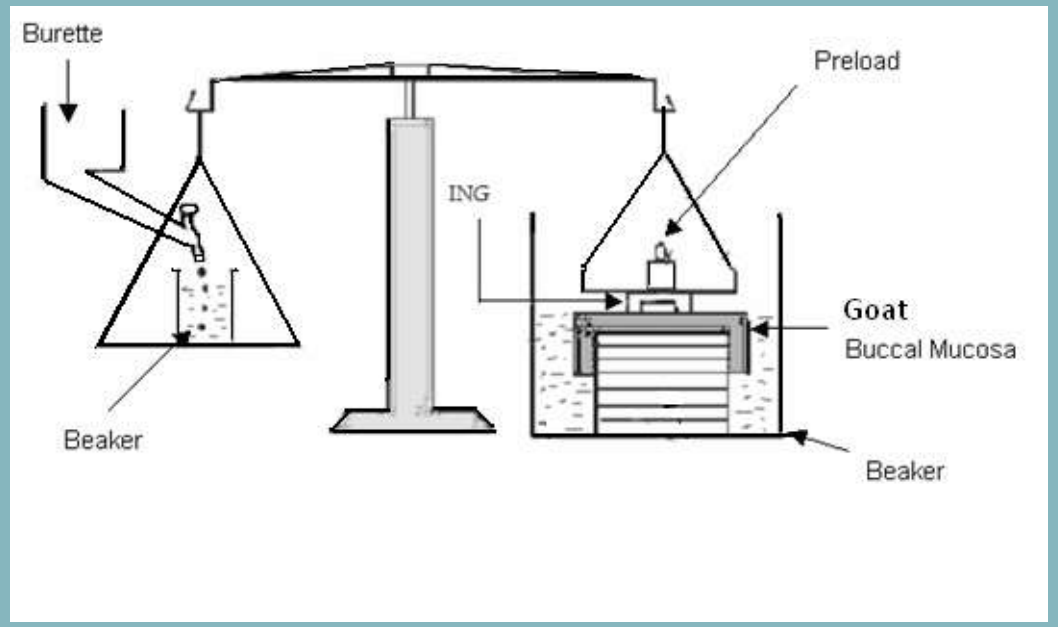


Mucoadhesion test

a) Modified Balance Method:

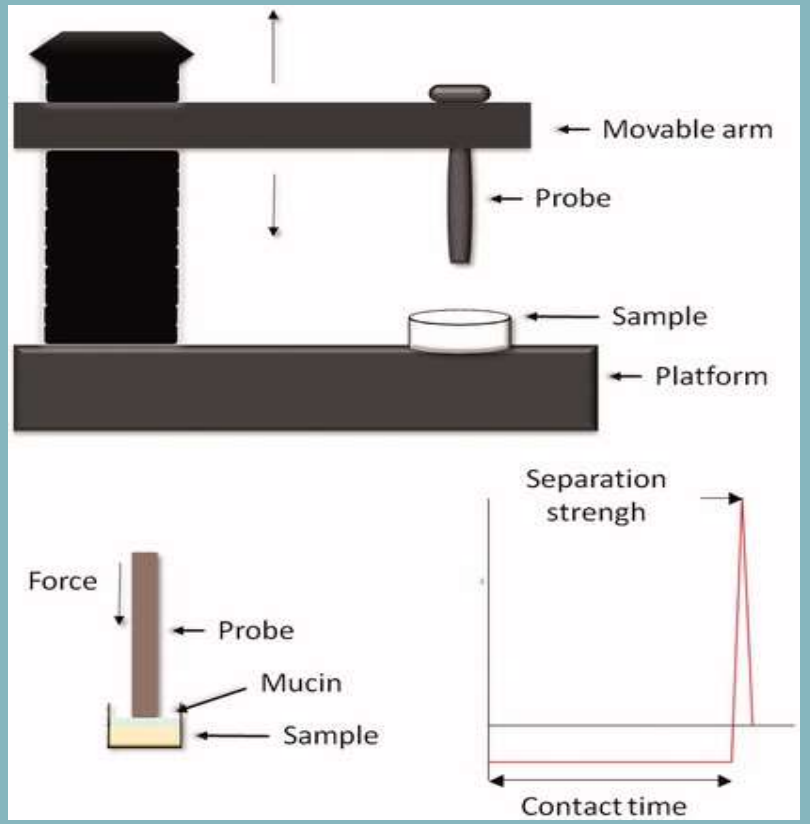
$Detachment\ force\ (dyne\ cm2\ ) = (m \times g)/A$

m : the required weight (g) for detachment,
g : the gravity acceleration (980 cm/s2),
A : the exposed tissue area (cm2)



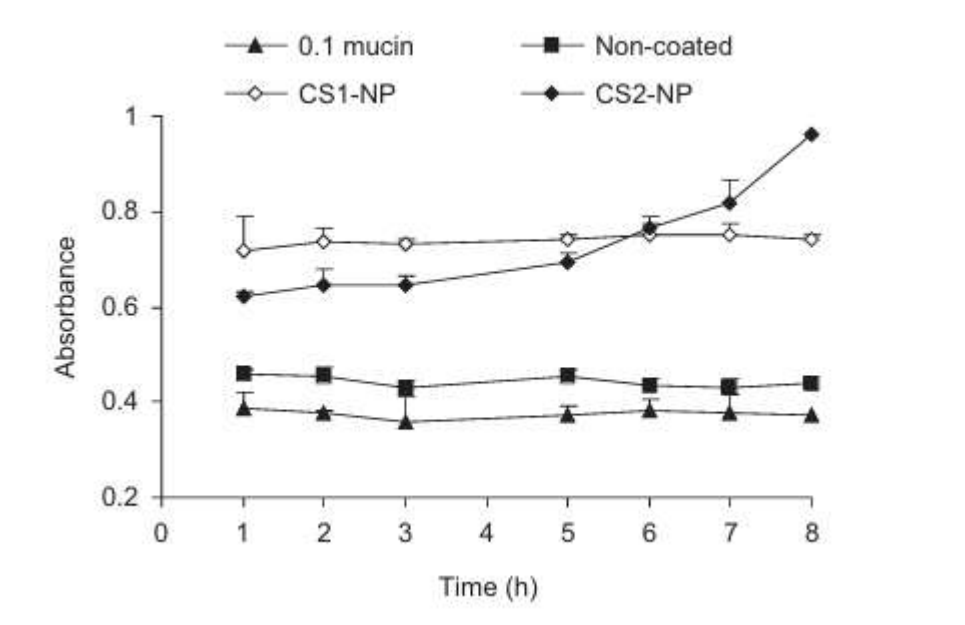
b) Texture Analyzer-Based Method:

1. Detachment force (g)
2. Work of adhesion (AUC, g/s)



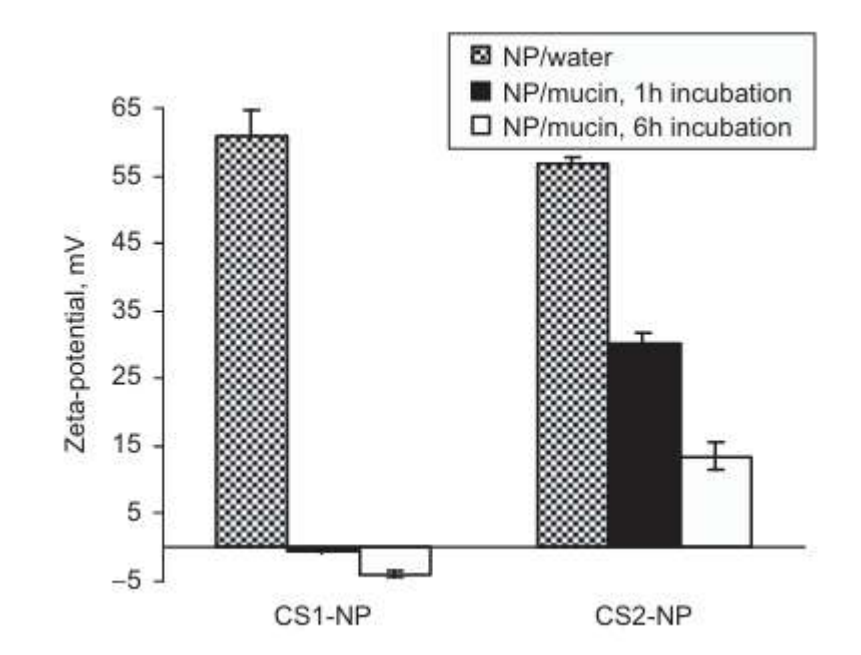
d) Turbidimetric Titration:

The UV-Vis spectrophotometer used to detect change in mucin absorption upon polymer adhesion.



e) Mucin Zeta potential method:

The change of surface charge density upon addition of charged mucoadhesive polymers.



f) Mucin Particle size method:

The change of the particle size due to aggregation and disaggregation of mucin particles was observed with dynamic light scattering measurements (Zetasizer).

Spray performance study

1. Tests based on **Weight determination**: focused on the weight of the formulation released per actuation and includes the following tests

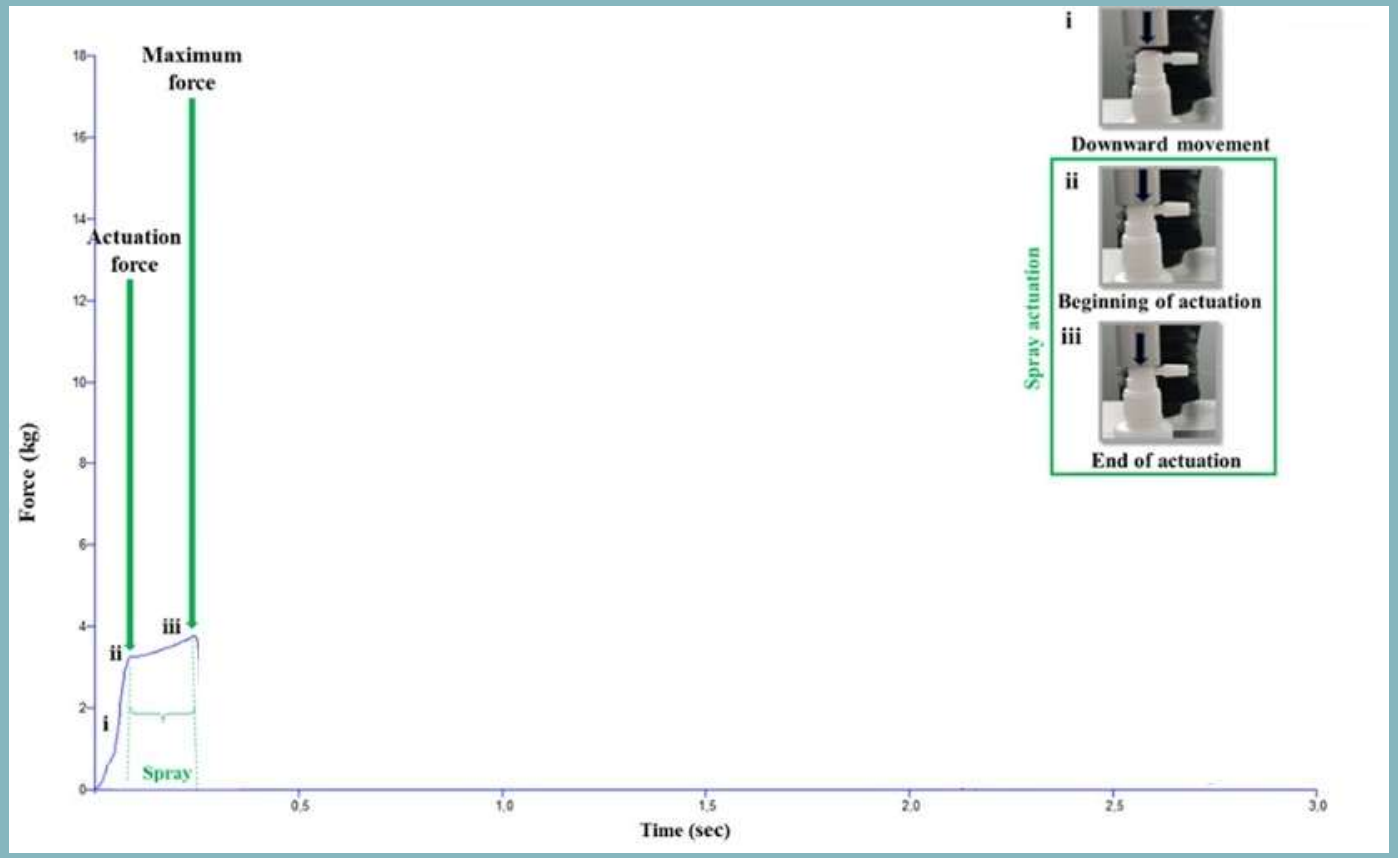
    a) Priming actuations,
    b) Shot weight determination,
    c) Pump delivery, and the number of in-use actuations.

2. Characterization of the **spray plume** and include:

    a) Spray angle
    b) Spray pattern,
    c) Plume geometry,
    d) Droplet size distribution.

Automated Spray Actuation

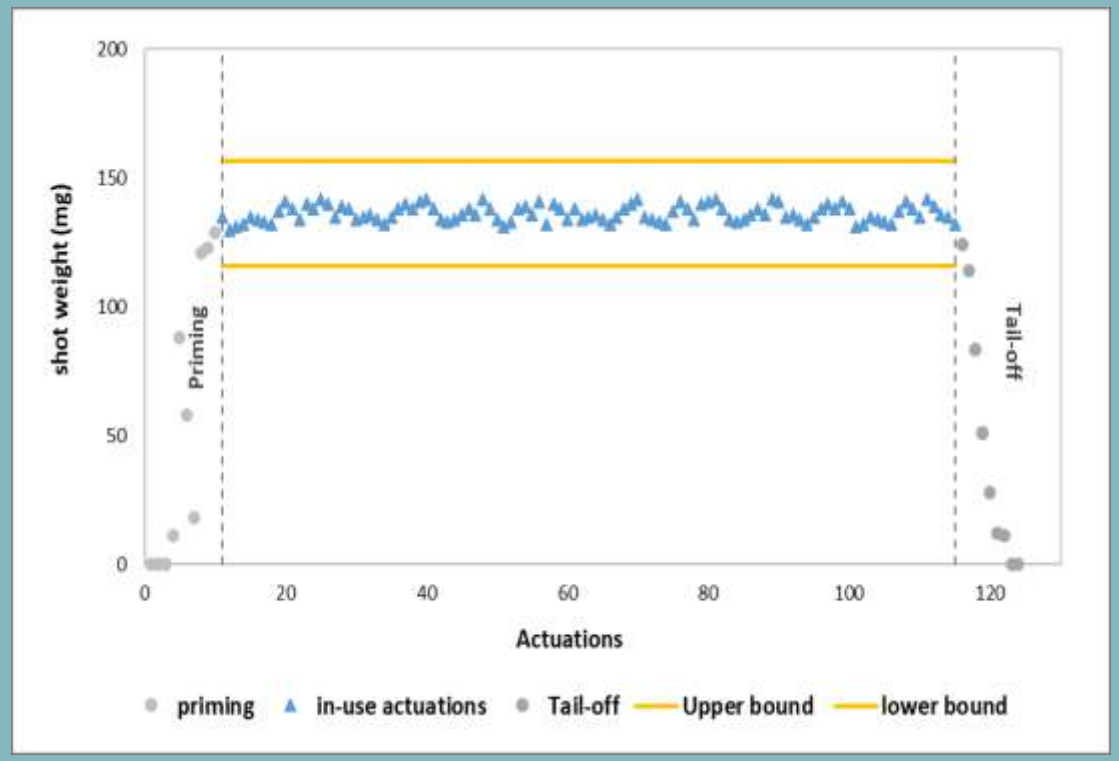
1. **Actuation force.**
2. **Maximum force.**



- acceptable actuation force is up to **5.8 kg** for adults and **3.4 kg** for pediatric.

Spray Dose Uniformity

- A sequential spray delivery profile includes three segments, and all based on pray shot weight determination.
  1. priming actuations,
  2. In-use actuations,
  3. Tail-off Actuations.
- **The weight of the individual actuations** must be **within ± 15%** of the target weight and their **mean within ± 10%,** considering the acceptance criteria by the FDA.
- Weight Loss %: the difference between the initial weight of spray device before actuations and the remaining weight after finishing the test.
- **Not more than 5% loss of weight**.



spray delivery profile

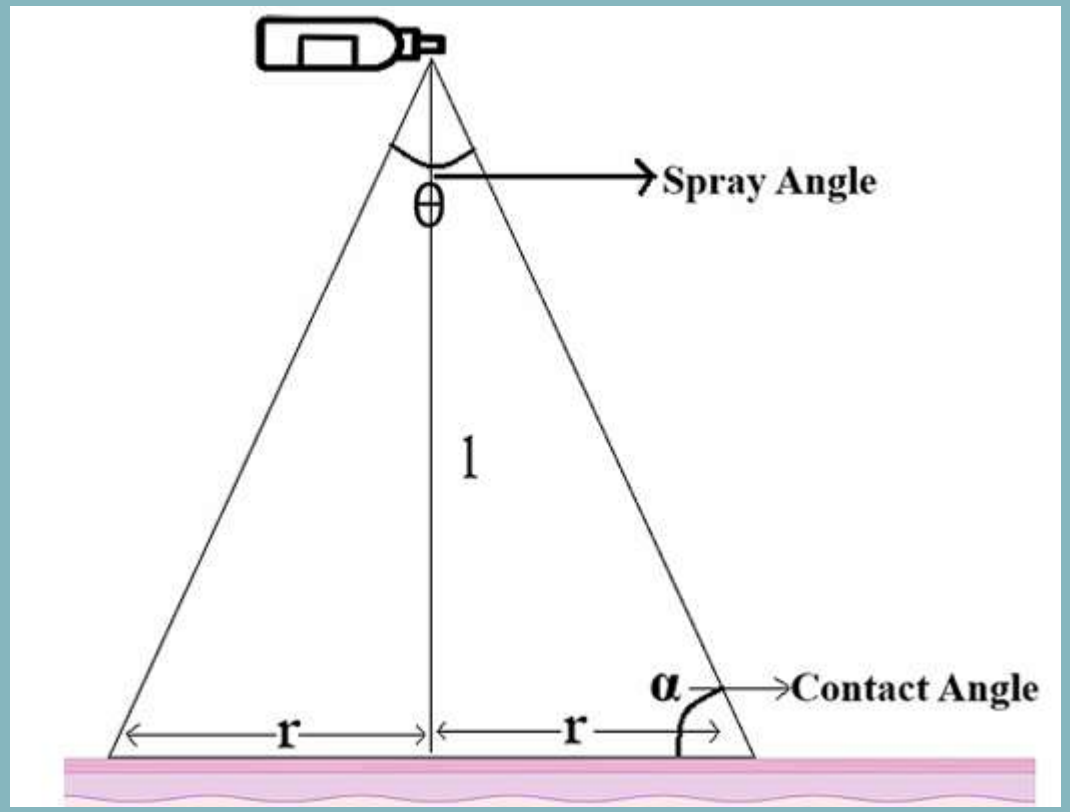
Spray Plume Characterization

1. Spray Angle

$\theta = 2 \tan^{-1} (r/l)$

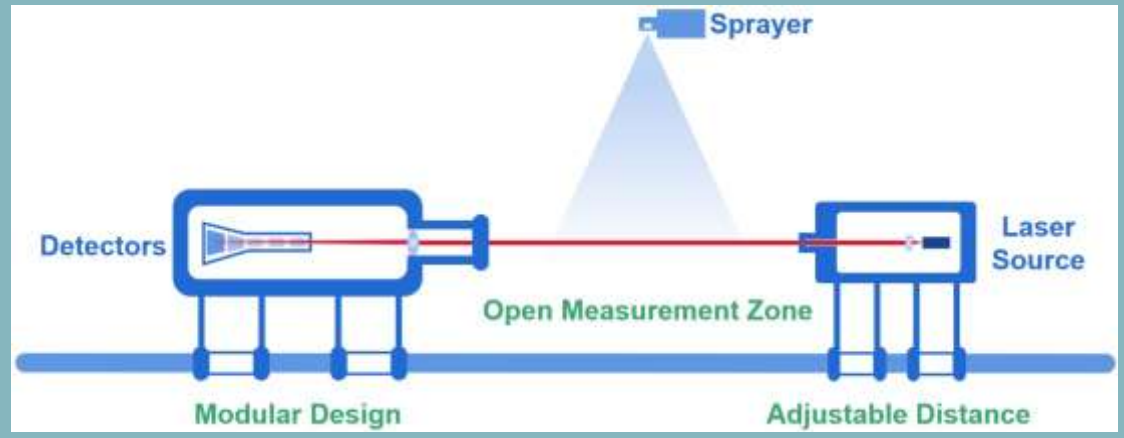
θ: spray angle,
r: radius of spray pattern,
l: nozzle height.

- Spray angle is inversely proportional with solution viscosity.



2. Spray pattern and plume geometry:

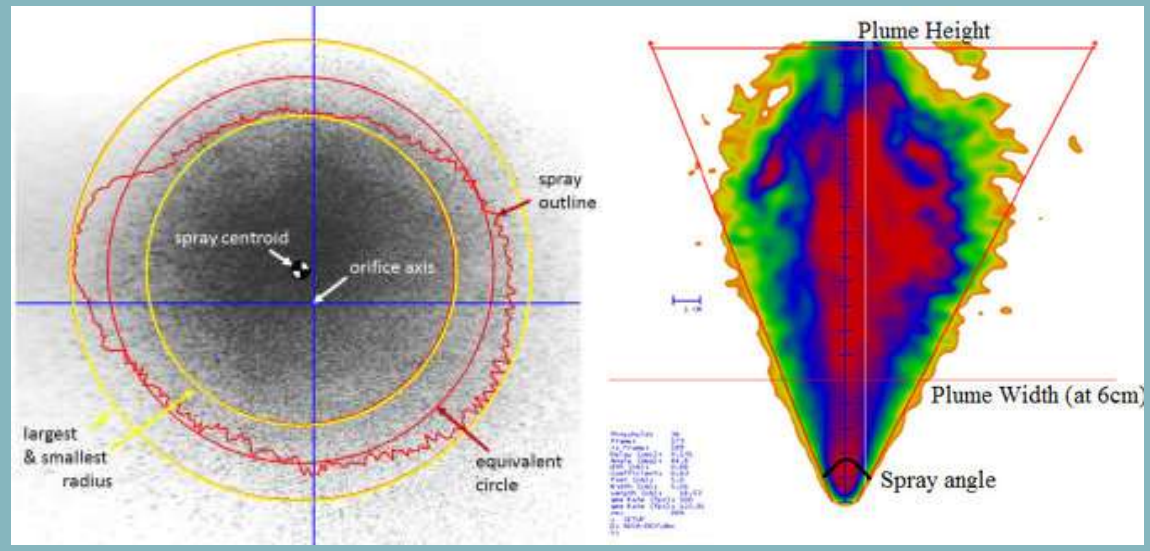
The spray plump is evaluated to maximum diameter (Dmax) and minimum diameter (Dmin) and the ovality ratio (Dmax/Dmin). **Ovality ratio close to 1 is desirable ,ensure uniform and more targeted application.**



3. Spray droplet size Distribution (DSD):

The droplet size is mainly influenced by the design and handling (i.e. actuation parameters) of the device, as well as by the formulation

According to the literature, **droplet sizes** must be higher than **>10 µm**, since below this value they can be inhaled into the lungs and cause toxicity.



Spray Stability Study

1. **Weight loss** upon storage (Container leakage).
2. Plume **weight uniformity**.
3. **pH**.
4. **Drug content** (API stability).

Thank You