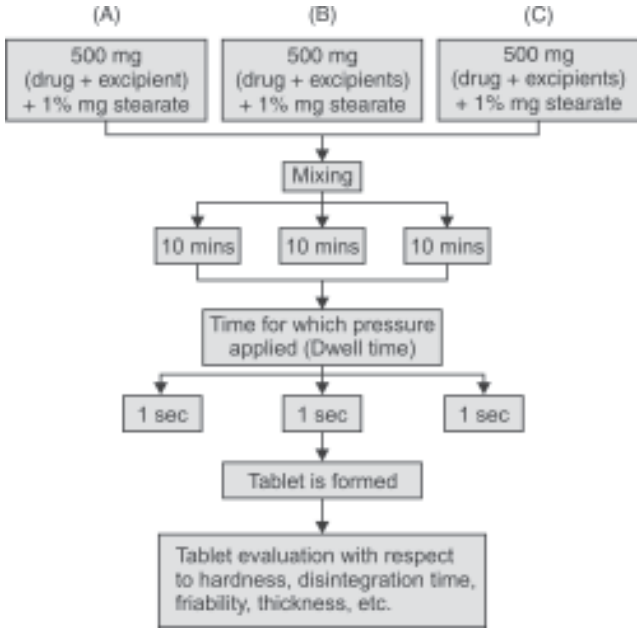
Method (A): Shows tablet formed by direct compression,

Method (B): Shows tablet formed by wet granulation and

Method (C): Shows tablet formed by dry granulation respectively.

Method of compression testing

Based on evaluation, process will be selected.



Crystallinity and Polymorphism

Crystal habit and internal structure of a drug can affect bulk and physicochemical properties which ranged from flowability to chemical stability.

Habit is described as the outer appearance of a crystal's internal structure in molecular arrangement within the solid.

Changes with internal structure usually alter the crystal habit. Chemical changes as conversion of a sodium salt to its free acid form produce both a change in internal structure and crystal habit.

Similarly, the solubility in pH region where free base is limiting is expressed as:

$$S_t,\ pH > pH_{max} = [BH^+] + [B]_s$$

$$= [B]_s \left(1 + \frac{H^+}{Ka}\right)$$

Corresponding equation for acidic compounds

$$S_t\ pH < pH_{max} = [AH]_s \left(1 + \frac{Ka}{[H^+]}\right)$$

$$S_t\ pH > pH_{max} = [A^-]_s \left(1 + \frac{H^+}{Ka}\right)$$

Since ionizable compounds may be available in free or salt form, one could use either in solubility experiments, e.g. phenazopyridine, free base, having pKa of 5.2, exhibits maximum solubility at pH 3.45 (pH_{max}) over pH range of total solubilities at pH_{max} region.

Solubility product/common ion effect

In a saturated solution of a salt with some undissolved solid, there exists an equilibrium between the excess solid and the ions resulting from the dissociation of the salt in solution. For a hydrochloride salt represented as BH^+Cl^-, the equilibrium is

$$BH^+Cl^-\ (s) \rightleftharpoons BH^+ + Cl^-$$

Where, B is the base compound, BH^+ and Cl^- represent hydrated ions in solution. The corresponding equilibrium constant K is given by

$$K = \frac{[BH^+][Cl^-]}{[BH^+Cl^-]_{solid}} \quad \ldots (1)$$

As a solid, the activity of $[BH^+Cl^-]_{solid}$ is constant, then equation becomes

$$K_{sp} = [BH^+]\ [Cl^-] \quad \ldots (2)$$

For an ionizable drug as mentioned earlier, total solubility S_T is sum total of $[BH^+]_s$ and [B] since $[BH^+]_s >> [B]$, equation (2) becomes,

$$K_{sp} = S_T\ [Cl]^- \quad \ldots (3)$$

the dissolution rate of a solid in its own solution is adequately described by Noyes-Nerest equation.

$$\frac{dC}{dt} = \frac{SD(C_s - C)}{hV}$$

where dC/dt= dissolution rate, S = surface area of dissolved solid, D = diffusion coefficient, C = solvent concentration in the bulk medium, h = diffusion layer thickness, V = volume of dissolved medium, C_s = solute concentration in the diffusion layer.

During early phase of dissolution, $C_s >> C$ and is essentially equal to saturation solubility C_s, surface area A and volume V can be held constant under this condition and at a constant temperature and agitation above equation becomes

$$\frac{dC}{dt} = KC_s \text{, where, } K = SD/hV = \text{constant}$$

Intrinsic dissolution rate is generally expressed as mg dissolved × ($min^{-1}cm^{-2}$)

This constant rate differs from the dissolution from conventional dosage form which is known as total dissolution (mg/min) where the exposed surface area (S) is uncontrolled as disintegration, deaggregation and dissolution process. According to the intrinsic dissolution rate, it is independent of formulation effects and measures the intrinsic properties of the drug and salt as a function of dissolution media effects, e.g. pH, ionic strength and counter ions.

Influence of some parameters on dissolution rate of drug:

- Diffusion coefficient of drug.
- Surface area of solid drug.
- Water/oil partition coefficient of drug.
- Concentration gradient.
- Thickness of stagnant layer.

Effect of temperature

The heat of solution, ΔH_s, represents the heat released or absorbed when a mole of solute is dissolved in a large quantity of solvent. Most commonly, the solution process is endo-

Table 1.13: Saturated salt with % RH below 40%

	Relative humidity (% RH)		
Temperature °C	*Lithium chloride*	*Potassium acetate*	*Magnesium chloride*
0	11.23 ± 0.54		33.66 ± 0.33
5	11.26 ± 0.47		33.60 ± 0.28
10	11.29 ± 0.41	23.28 ± 0.53	33.47 ± 0.24
15	11.30 ± 0.35	23.40 ± 0.32	33.30 ± 0.21
20	11.31 ± 0.31	23.11 ± 0.25	33.07 ± 0.18
25	11.30 ± 0.27	22.51 ± 0.32	32.78 ± 0.16
30	11.28 ± 0.24	21.61 ± 0.53	32.44 ± 0.14
35	11.25 ± 0.22		32.05 ± 0.13
40	11.21 ± 0.21		31.60 ± 0.13
45	11.16 ± 0.21		31.10 ± 0.13
50	11.10 ± 0.22		30.54 ± 0.13
55	11.03 ± 0.23		29.93 ± 0.16
60	10.95 ± 0.26		29.26 ± 0.18
65	10.86 ±0.29		28.54 ± 0.21
70	10.75 ± 0.33		27.77 ± 0.25
75	10.64 ± 0.38		26.94 ± 0.29
80	10.51 ± 0.44		26.05 ± 0.34
85	10.38 ± 0.51		25.11 ±0.39
90	10.23 ± 0.59		24.12 ± 0.46
95	10.07 ± 0.67		23.07 ± 0.52
100	9.90 ± 0.77		21.97 ± 0.60

Incompatibility between excipient and drug substance can be detected by:

1. Differential scanning chromatography.
2. By evaluating organoleptic characteristics like change in color.
3. By checking purity of drug substance using HPLC method.

1. Differential scanning chromatography: Differential scanning chromatography can be used to investigate and predict any physicochemical interaction between components in a formulation and, therefore, can be applied to the selection of suitable chemically compatible excipients. For example, in one of the studies, compatibility of oxcarbazepine (OXC) with excipients was done using DSC analysis. DSC compatibility