

Specificity and Discriminatory Challenges Leading to Limitation in Accurate Complete Identification and Quantification of Excipients in RLD Deformulation

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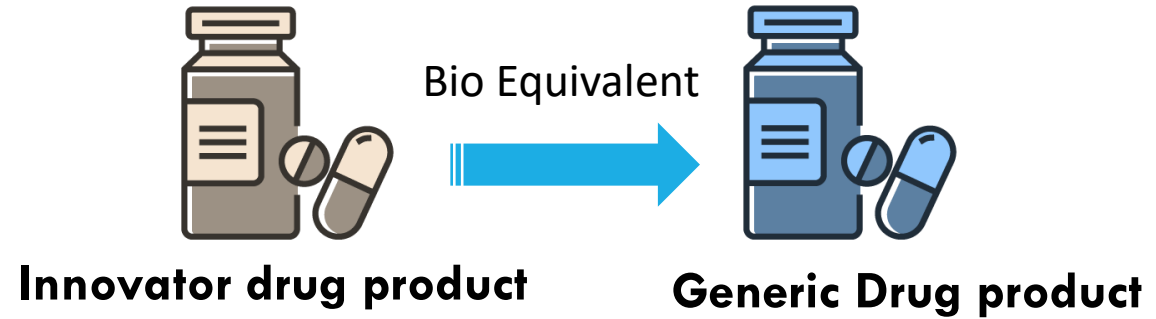
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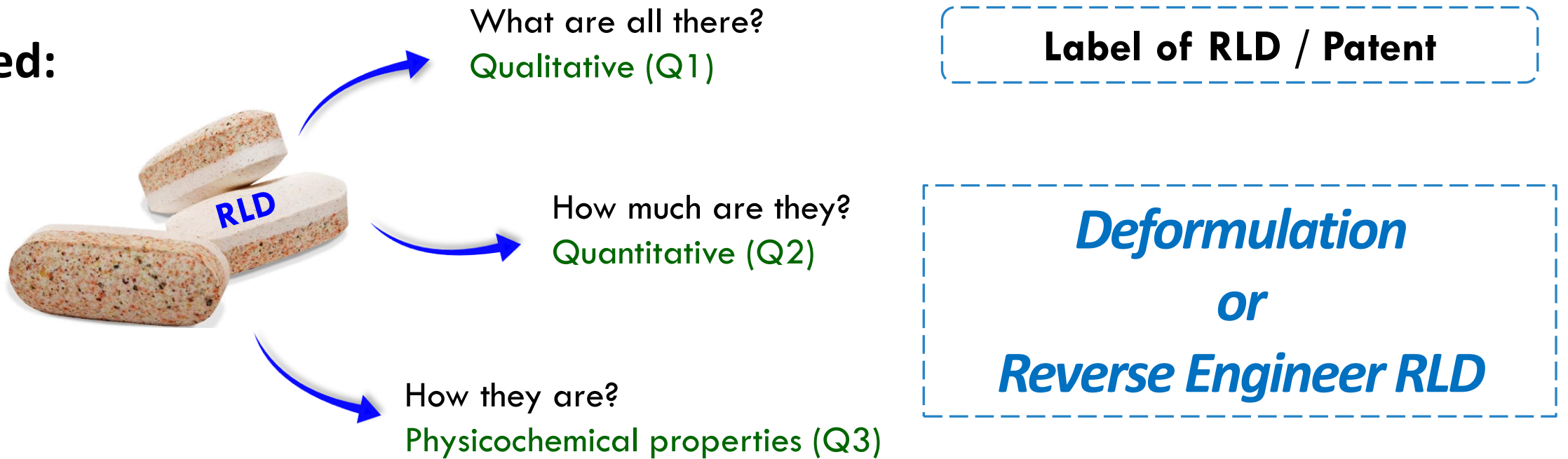
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Goal: Bio Equivalent Product

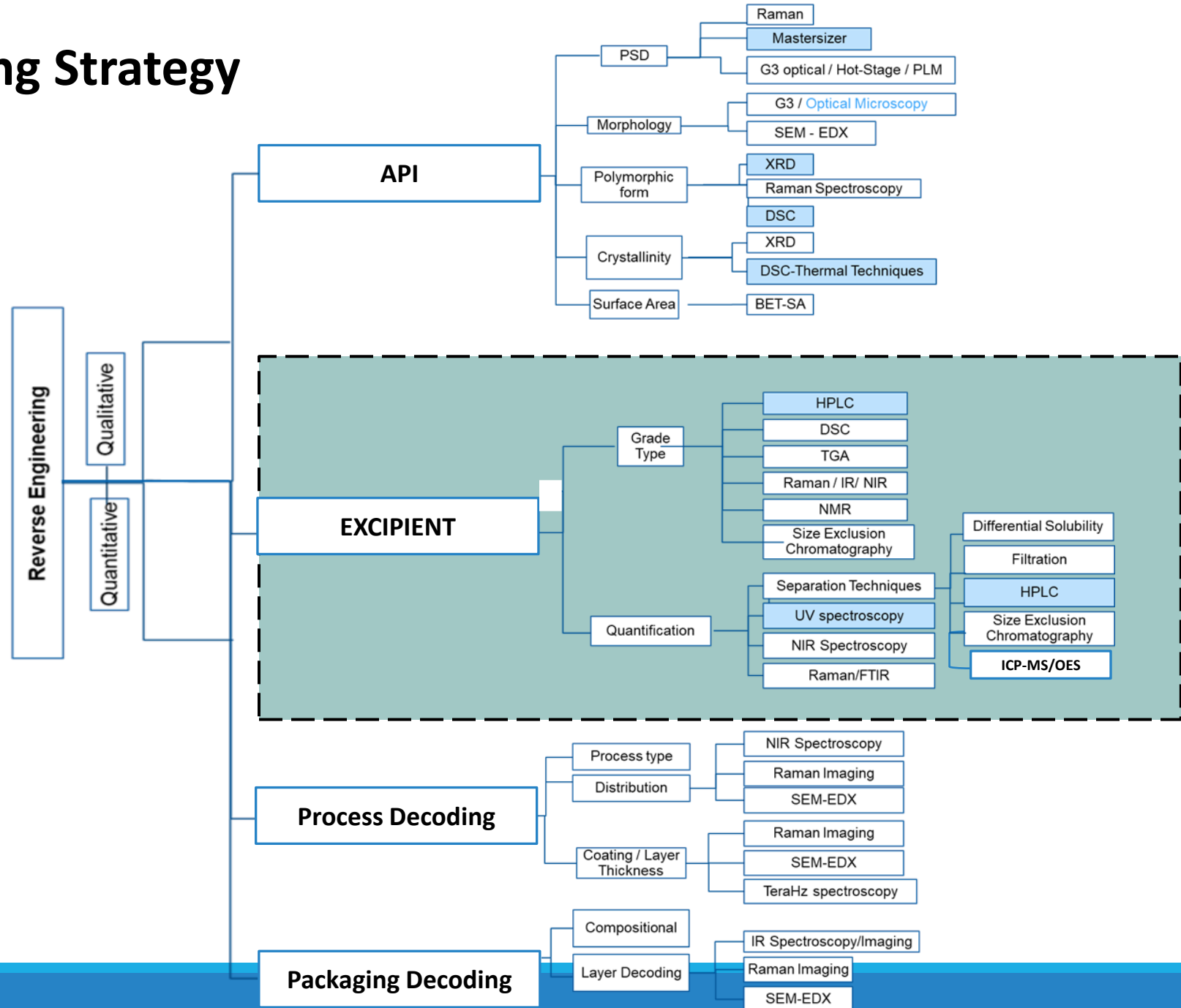


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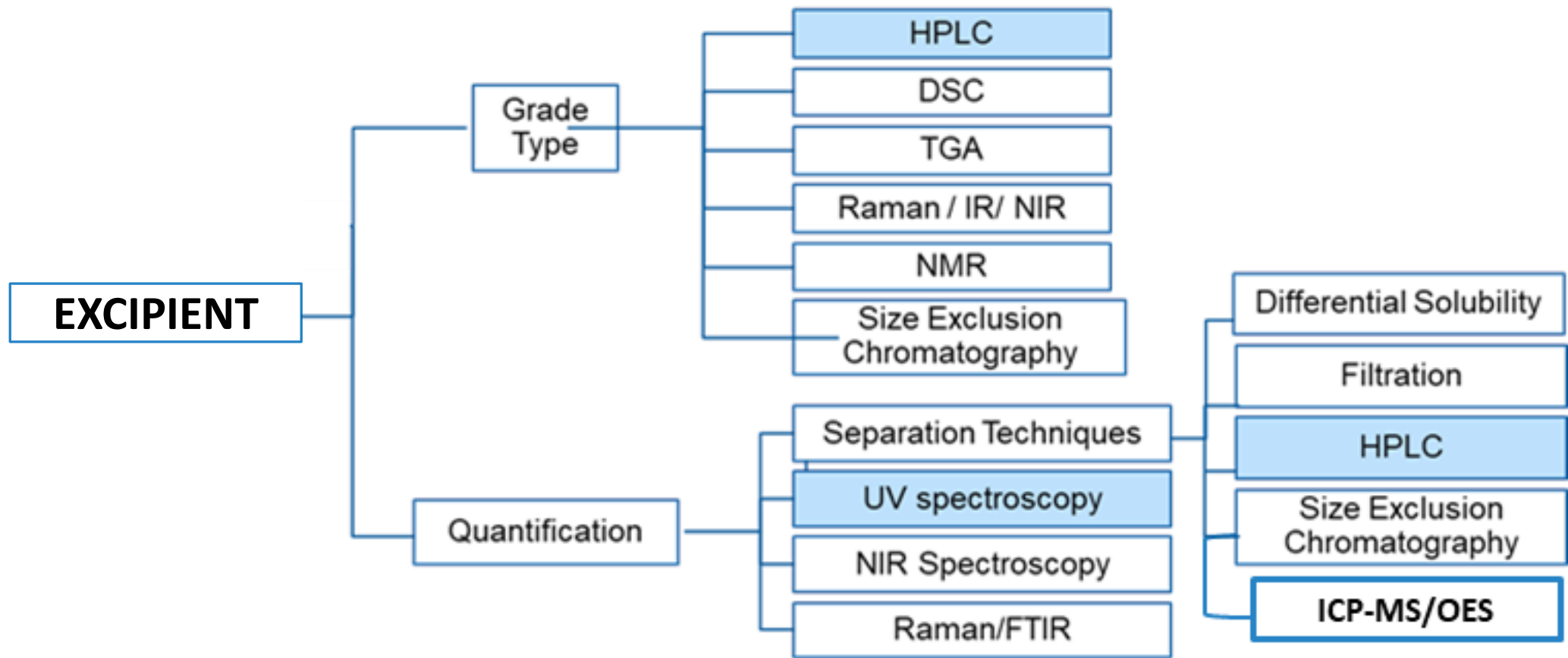
Reverse Engineering Strategy



Excipient Deformulation

Challenges : **Qualitative (Q1) & Quantitative (Q2)**

- Polymer Grade Identification and Quantification – Selectivity issues
- Co-polymer quantification and its ratio
- Absolute Quantification of Excipients like CCS, Mg Stearate, SLS, Talc etc
- Process Impact on Polymer and hence true identification of the excipient
- Surfactant identification and Quantification
- Challenges in method due to ineffective extraction of the component



- Polymers (PVP, HPMC etc.): GPC with special detectors etc.
- Organic small molecules (Mannitol, Lactose): LC/GC with special detectors
- Salts/Inorganic compounds(SSG, Silica): ICP-MS/OES, IC etc.
- Other excipients: Specific techniques

Traditional Approaches

➤ Separation technique QUANTIFICATION

- differential solubility,
- filtration (with filters of a specific pore size or molecular weight cutoff),
- high-performance liquid chromatography (HPLC), high-performance thin-layer chromatography (HPTLC), and
- size-exclusion chromatography (SEC) / GPC

➤ Indirect / Alternate approach –

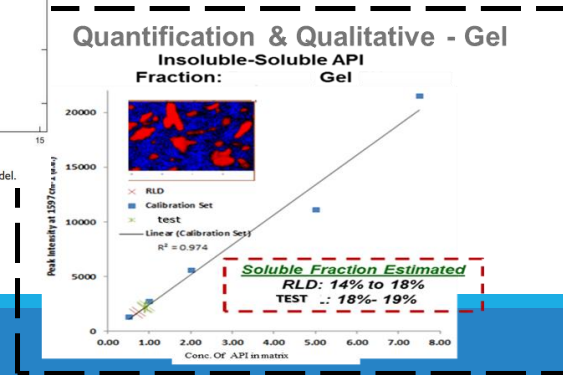
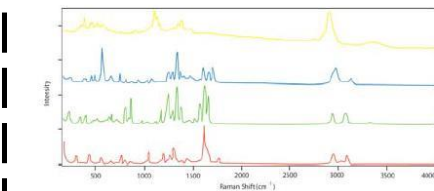
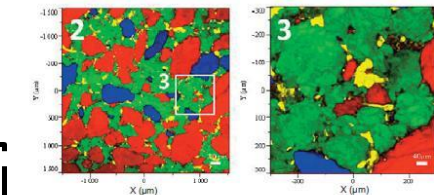
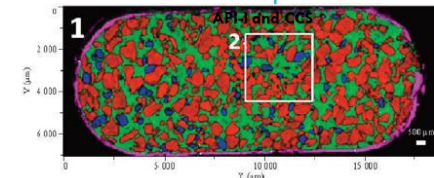
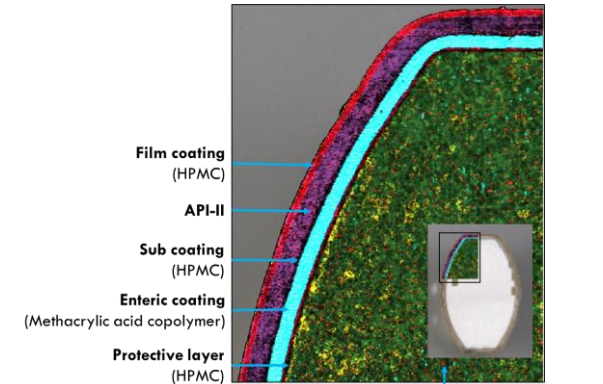
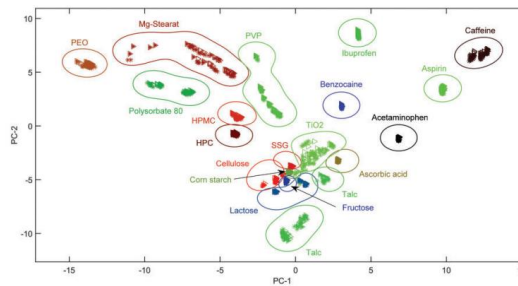
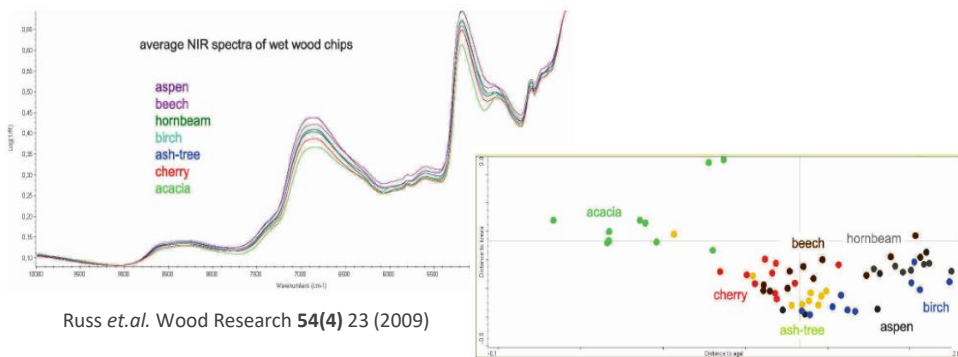
- Analyzing Anion: Example: CCS, Mg Stearate, SLS, Talc etc..
- Example: 2 component with same element – for example Talc and Mg stearate, then Mg Stearate quantification not possible by ICP MS, in that case stearic acid quantification for Mg stearate & Si for talc.

Alternate Approach...

➤ Spectroscopy based Method - NIR or RAMAN or FTIR + Chemometrics

Examples:

1. HPMC grade identification through FTIR
2. Example: MCC quantification Similarity through NIR in Tablet (Market Extension)
3. Example: Quantification in Gel (example done in case of a gel for solubilized API & insoluble API)
4. Identification using Imaging Techniques in layers of tablet; in Globules for emulsions,



Conclusion

- Specificity and Discriminatory remains a challenges
- Alternate technology to be used
- Orthogonal technique together can provide more insight and understanding of the inactive excipients

Thank You