



Pharmaceutical Formulation & Manufacture

**In-line spectroscopy for HME applications &
Amorphous Solid Dispersions**



 **COLVISTEC**
Inline Process Monitoring

- **ColVisTec AG**, Max-Planck-Str. 3, 12489 Berlin, Germany
- Founded in 2009
- Specialists in *in-line* spectroscopy PAT tools for pharmaceutical process monitoring
- Focused on PAT applications for pharmaceutical
 - Hot-Melt Extrusion,
 - Wet Granulation,
 - Amorphous Solid Dispersion
- ColVisTec team consists of 16 employees
- Funded by „Horizon 2020 Project“ (IMPAX)
- **HIRING!!!** Actively looking for talent to help us grow

Hot Melt Extrusion (HME)

Continuously monitor and improve manufacturing process;
assure consistent product quality



Hot Melt Extrusion (HME)

Reduce

- Operational uncertainty & risk
- Batch failures and product recalls
- Manufacturing costs & time
- Time for research & development phases

Improve

- Process understanding and robustness
- Continuous quality assurance
- Regulatory flexibility
- Dissolution rate and bioavailability of poorly water soluble API

Typical Experimental Setup



Extrudate CQA

Qualitative parameters:

- Appearance
- API Solubility / oversaturation
- Content uniformity / moisture content

Quantitative parameters:

- Colour
- Concentration
- Stability / degradation

Piroxicam Case Study

- UV-Vis absorption spectra used to construct calibration model
- Determine saturation threshold & drug loading maxima
- By tracking the calculated colour parameter “b*”, can directly observe spectral changes in solid extrudates.
- Continuous monitoring of extrudate API content

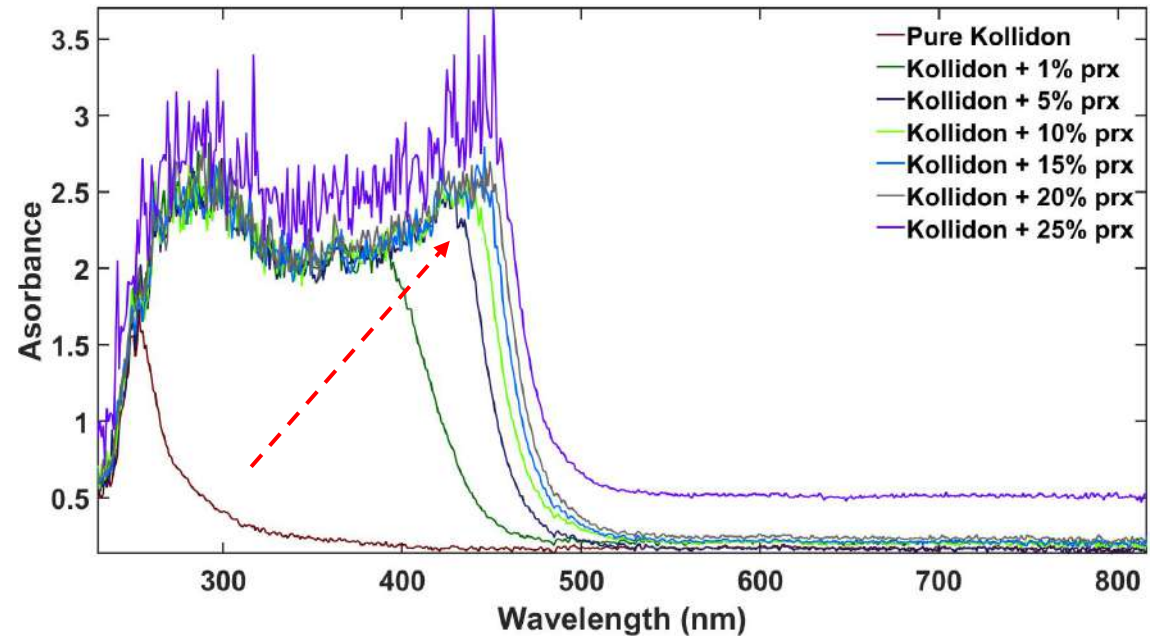
Piroxicam can be converted to an amorphous form to achieve higher physical stability and overall solubility

Good thermal stability at the extrusion temperature used, defines the lower end of the processing window

**Case study : Hot Melt Extrusion of Piroxicam
in Soluplus / Kollidon VA64 polymers**

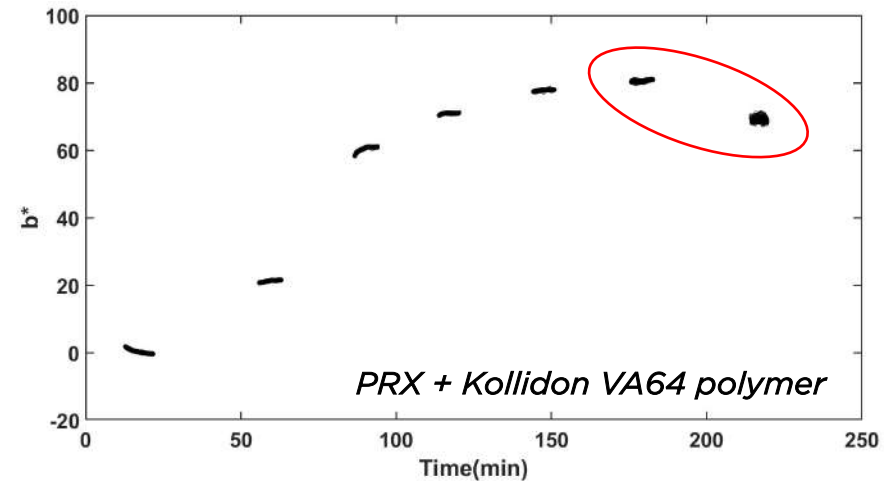
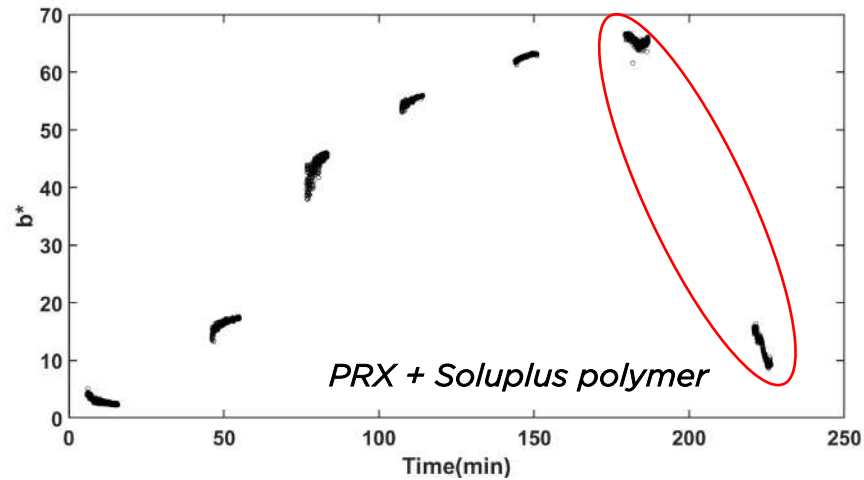
In-line UV-Vis spectra from
Piroxicam / polymer extrudates

Red arrow indicates direction of
absorption shift, proportional to
API loading



Case study : Hot Melt Extrusion of Piroxicam in Soluplus / Kollidon VA64 polymers

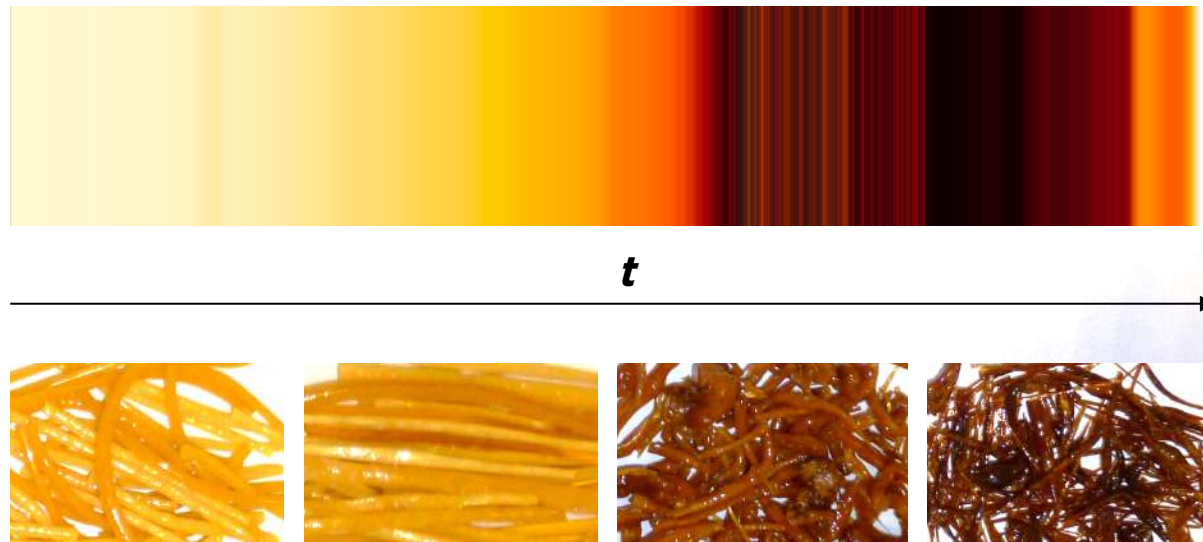
- Partial-Least-Square regression work-up of Piroxicam spectral data produced a robust concentration model
- Calculate theoretical Piroxicam concentrations (in similar extrudates)
- Calculate formulation saturation threshold



SpecViewer

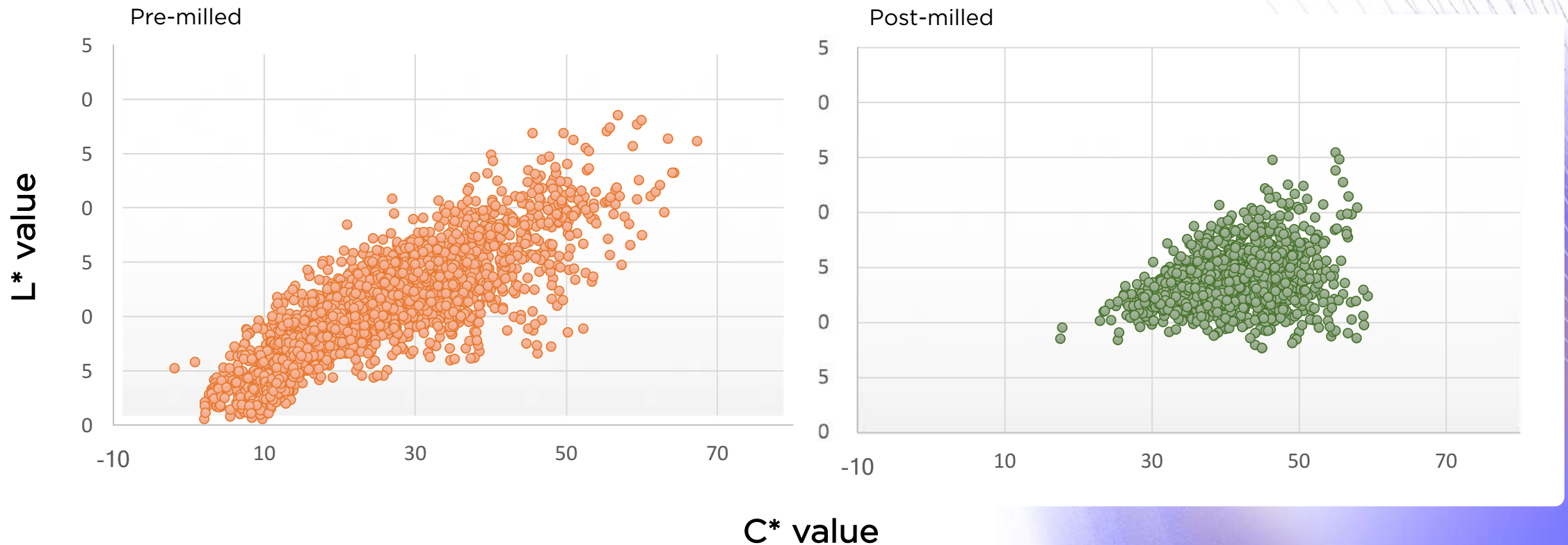
The SpecViewer software module allows live spectral data to be viewed as a “colour time-course”

A mathematically-derived colour representation of all Visible absorption spectra.



API powder milling - Particle analysis by UV-Vis spectroscopy

Measure and monitor changes in API powder properties using Lightness (L^*) / Brightness (C^*) values, calculated from UV-Vis spectra





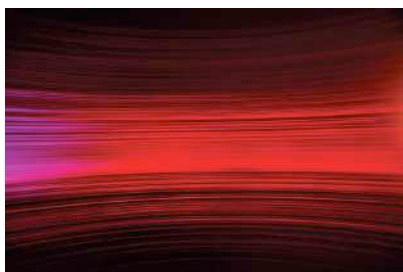
Co-funded by the Horizon 2020 programme
of the European Union



IMPAX - Inline/Instant Measurement for Pharma eXtrusion

IMPAX - a new multi-spectrum integrated PAT system

Simultaneous *in-line* measurement using:



NIR 800-2000 nm

- Measure moisture content & drying processes
- Characterize raw materials & feedstocks
- Study blend uniformity
- Finished product ID & specification



UV-VIS

- Accurate quantification of API
- Study API dissolution kinetics
- Assess impurity profile in chemical feedstocks
- Measure thermal stability & API / polymer degradation kinetics
- Monitor process deviations, intervene & rescue



RAMAN 780 or 830 nm

- Measure compound crystallization state
- Track specific impurities
- Finished product ID & specification



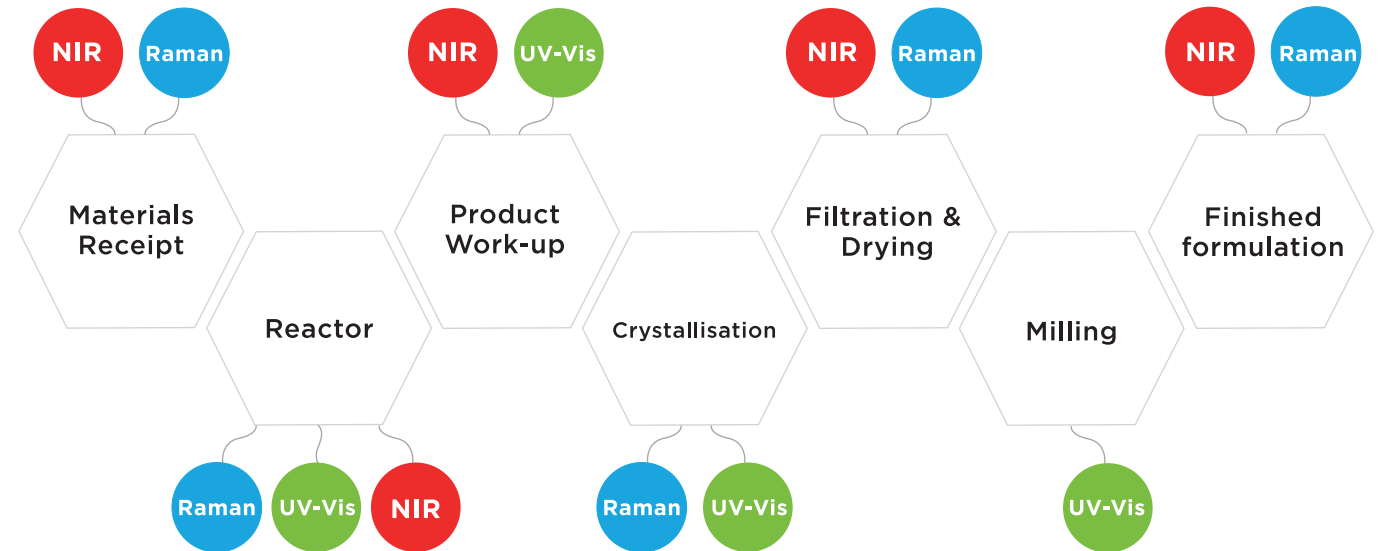
IMPAX - a new multi-spectrum integrated PAT system

Simultaneous *in-line* measurement using:

	NIR	Raman	UV-Vis
Origin	Changes in hydrogen bonding	Vibrations and Rotations in ground state molecules generated by inelastic collisions of activated molecules	Changes in π -electron system
Interpretation	Quite complex, overtones, overlapping bands	Complex	Simple
Characteristics	Specific, complex modeling Not interactive	Very specific, low sensitivity, possibility for sample damage Laser safety issues	Not very specific Highly sensitive, Intuitive, interactive
Costs	Low to very high (full range)	High	Low

IMPAX represents the first production monitoring platform to combine three spectroscopy types (**UV-VIS**, **NIR**, AND **RAMAN**) into one system.

From raw materials to finished product, the **IMPAX** system supports every stage of the pharmaceutical manufacturing process.



The IMPAX system comprises:

- cGMP compliant materials, hardware & software
- Proprietary, optimised probes & optical fibres designed for compatibility with various industrial extruder types
- Single user terminal & interface for all three spectrometers, with centralised data processing & communications
- Insulated against temperature variances and vibrations
- Small footprint, designed for easy disassembly & cleaning





Thank you!

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