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# Transmission Raman Microscopy as a Process Analytical Technique for Drug-loaded Hydralese (PGSU) Elastomers

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## PURPOSE

Long-acting implantables (LAIs) have become increasingly important in providing novel formulations for active pharmaceutical ingredients (APIs). Secant Group's Hydralese™ (poly(glycerol sebacate) urethane) (PGSU) is a novel, biodegradable elastomer that may be used for next-generation LAIs. PGSU is unique in its ability to provide linear release kinetics, high drug loading (often >60% w/w), and a surface-eroding degradation mechanism that minimizes burst release. Furthermore, PGSU maintains high flexibility, biocompatibility, and shelf stability under ambient conditions.

Increasingly, LAIs are in demand to deliver high potency APIs, which require a corresponding level of control over content uniformity and drug loading. Furthermore, developing new analytical technologies that are fast and easy to insert into manufacturing processes can lead to improved manufacturing capabilities, throughput, and quality. Raman spectroscopy is one such technique that allows users to non-destructively detect a molecular fingerprint of a sample material. From this data, information regarding composition, crystallization, and even stress/strain state can be derived and utilized for characterization. This technique is emerging in several industries due to its non-destructive nature, the specificity and sharpness of Raman bands, and compatibility with aqueous environments. Additionally, new variants of Raman microscopy, such as transmission and confocal Raman, offer bulk analysis of materials that were limited to surface measurements in traditional backscatter-based methods.

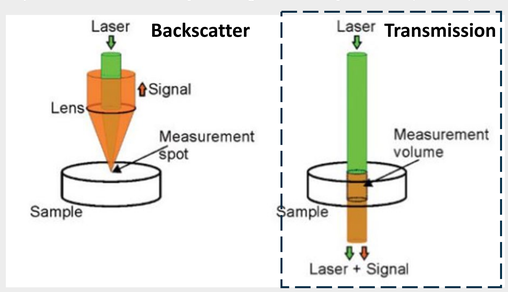
## OBJECTIVE

The objective of this study was to evaluate transmission Raman microscopy as a process analytical technique for the manufacturing of drug-loaded PGSU rods. Implantable, drug-loaded PGSU rods can be manufactured using reaction injection molding methods. In this study, rods were manufactured using 2'-deoxyadenosine as a model drug.

## METHODS

PGS resin polyol (Secant Group) was utilized to manufacture drug-loaded Hydralese (PGSU) rods with approximately 3mm diameter. A typical rod formulation consisted of 50% w/w 2'-deoxyadenosine. Rods were manufactured using reaction injection molding techniques using a two-component polyol-isocyanate urethane reaction chemistry to form Hydralese (PGSU).

A Raman microscope (InVia, Renishaw, Wotton-under-Edge, England, UK) equipped with a 785nm laser was utilized to analyze drug-loaded Hydralese rod samples. Samples were analyzed in transmission mode with various laser powers and exposure times. Rods were mapped by analyzing various points along their length to determine a metric of drug content. Raman spectra were quantified using a univariate analysis approach analyzing area under the curve (AUC) of the peak at 1585 $cm^{-1}$. Average AUC and relative standard deviation (RSD) were determined and used to analyze intra-sample content uniformity in drug-loaded Hydralese (PGSU) rods.




## RESULTS

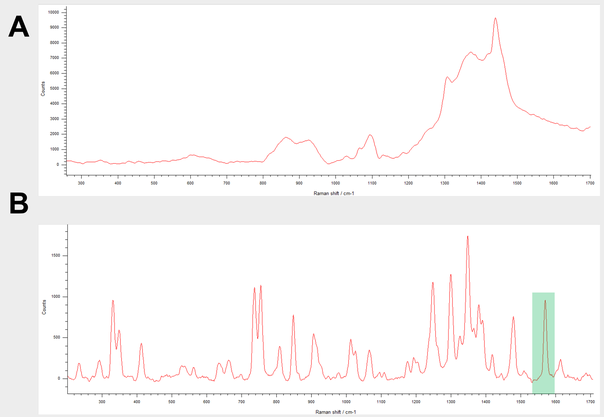
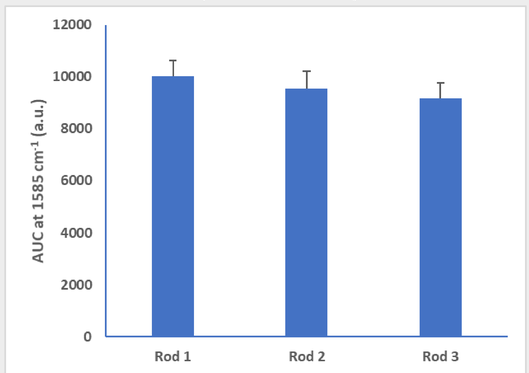



**Figure 1**. Raman spectrum of neat PGSU (A) and of neat 2'-deoxyadenosine (B). Green overlay indicates the 1585 $cm^{-1}$ peak used for analysis.




| | Intra-Rod | Batch |
|---|---|---|
| **Average** | See chart | 9574.6 |
| **RSD** | 6.46% | 4.58% |

**Figure 2**. Content uniformity of 2'-deoxyadenosine loaded-PGSU rods. Intra-rod and batch average signal and standard deviation are shown as metrics of drug loading.

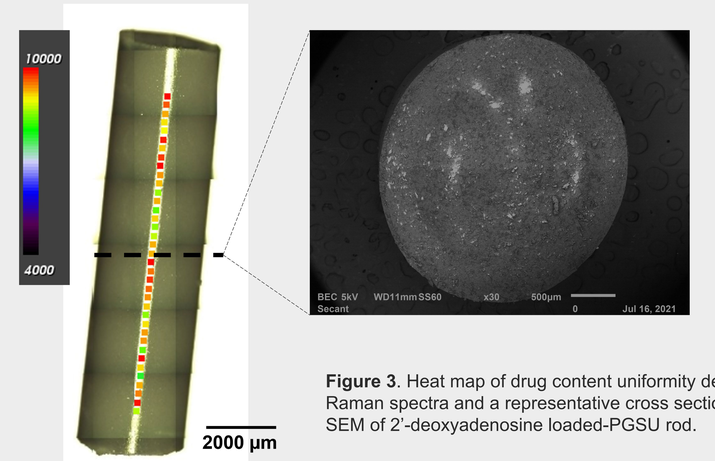



**Figure 3**. Heat map of drug content uniformity derived from Raman spectra and a representative cross section under SEM of 2'-deoxyadenosine loaded-PGSU rod.

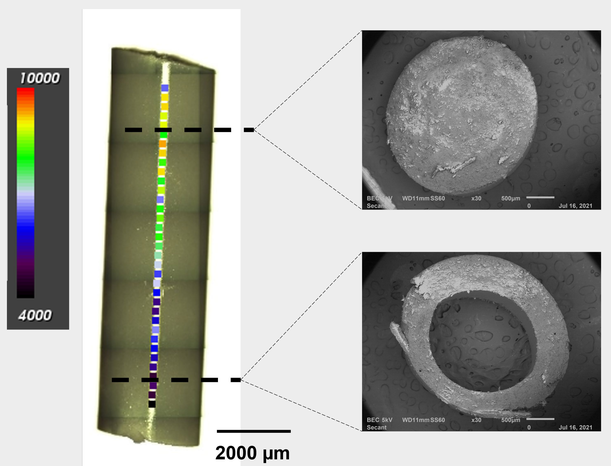



**Figure 4**. Heat map of drug content uniformity derived from Raman spectra of 2'-deoxyadenosine loaded-PGSU rod with internal defects. Regions with low Raman signal correspond to cross sections visualized with possible air bubbles or void spaces while regions with high Raman signal correspond with normal rod architecture.

## CONCLUSIONS

Transmission Raman analysis was shown to be a useful process analytical technique for drug-loaded Hydralese (PGSU) rods. Raman methods were utilized to successfully analyze drug content uniformity as well as detect defects in drug-loaded Hydralese (PGSU) implantable rods.

## REFERENCES

Reed, S., inventor; Secant Group, assignee. Tunable, controlled-release, urethane-containing elastomers and processes of forming the same. US patent US10918764B2.

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