Development of Poly(caprolactone) (PCL)-Based Polymeric Implantable Devices for Schizophrenia Treatment

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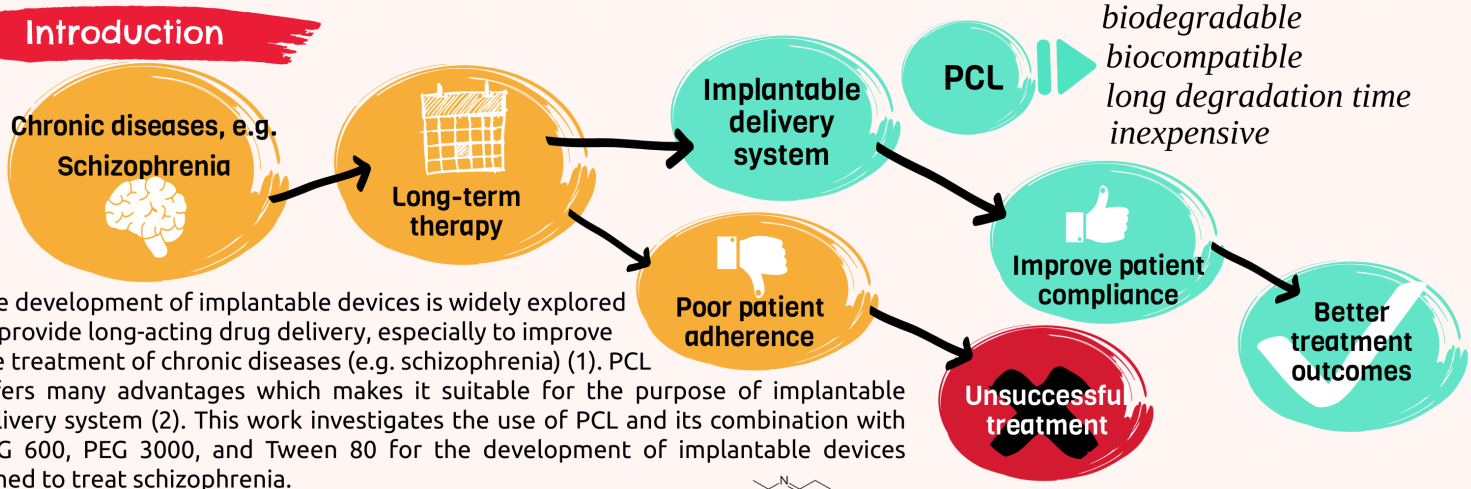
Introduction

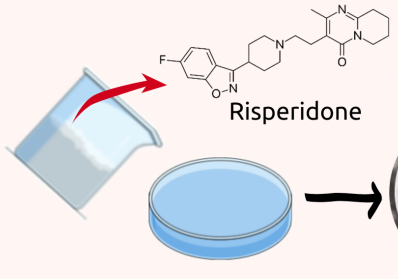


The development of implantable devices is widely explored to provide long-acting drug delivery, especially to improve the treatment of chronic diseases (e.g. schizophrenia) (1). PCL offers many advantages which makes it suitable for the purpose of implantable delivery system (2). This work investigates the use of PCL and its combination with PEG 600, PEG 3000, and Tween 80 for the development of implantable devices aimed to treat schizophrenia.

Methods

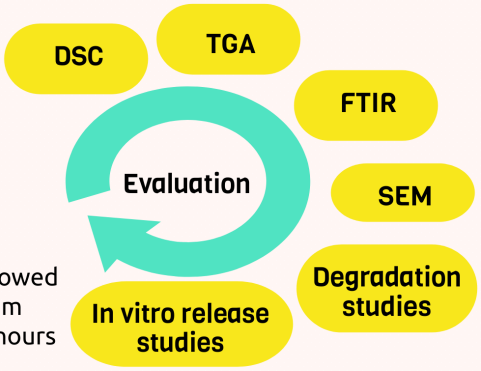
Compositions of PCL-based implants (%w/w)

Formula	RIS	PCL	Additional Substances	DCM
IMP1	20%	20%	-	60%
IMP2	20%	10%	PEG 600 10%	60%
IMP3	20%	10%	PEG 3000 10%	60%
IMP4	20%	10%	Tween 80 10%	60%

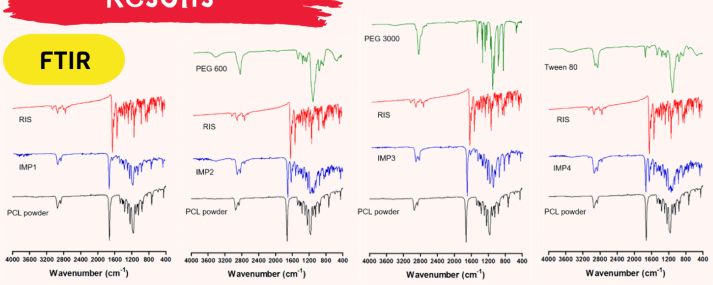


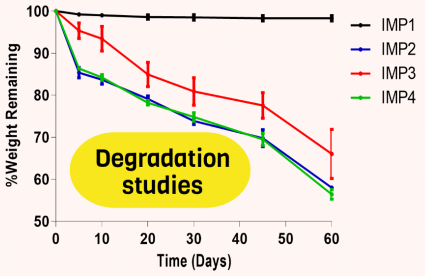
The polymer and drug mixture in DCM was poured in a petri dish

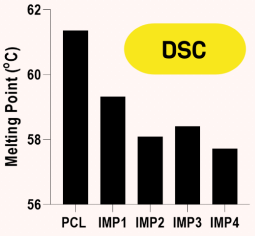
The implant was allowed to solidify in room temperature for 6 hours

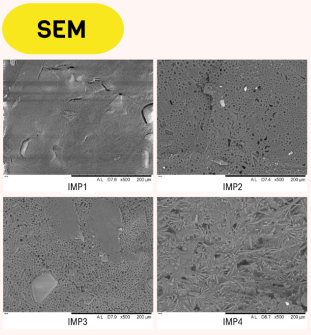


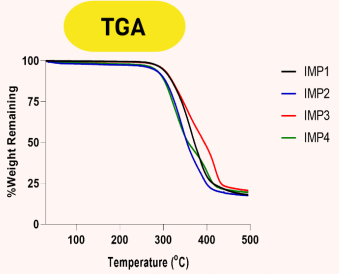
Results

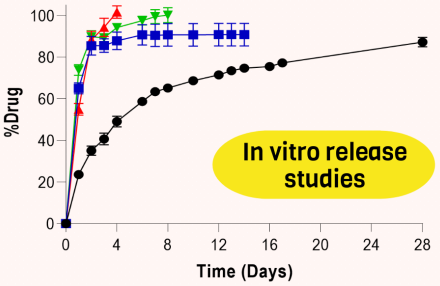












Formulations	Drug Release Rate (mg/day)
IMP1	8.73 ± 0.24 (day 0 – 6) 1.17 ± 0.07 (day 6 – 28)
IMP2	16.80 ± 2.52 (day 0 – 4) 0.17 ± 0.11 (day 4 – 14)
IMP3	19.5 ± 1.50 (day 0 – 4)
IMP4	25.87 ± 0.17 (day 0 – 3) 1.89 ± 0.93 (day 3 – 8)

The prepared implants were solid and flexible. Importantly, no new chemical bonds were observed between any of the components and that the addition of excipients modified the properties of the resulting implants as can be seen in DSC and TGA results, as well as degradation kinetics and release studies The average release rate of IMP1 was 1.17 ± 0.07 mg/day, which will be clinically relevant as the recommended dose of RIS for schizophrenia is 1-2 mg/day.

Conclusion

In this work, monolithic implants containing RIS were successfully fabricated using a solvent-casting method. Based on the results obtained, the addition of hydrophilic and amphiphilic compounds modified the properties of the implant, including the drug release rate. Based on results obtained in the *in vitro* release studies, it can be concluded that implants made of PCL showed the more sustained release profile providing up to 28 days.

References

1. Kumar, A. and Pillai, J. (2018) 'Implantable drug delivery systems: An overview', in *Nanostructures for the Engineering of Cells, Tissues and Organs: From Design to Applications*, pp. 473–511. doi: 10.1016/B978-0-12-813665-2.00013-2.
2. Malikmammadov, E. *et al.* (2018) *PCL and PCL-based materials in biomedical applications, Journal of Biomaterials Science, Polymer Edition.* Taylor & Francis. doi: 10.1080/09205063.2017.1394711.