

# Influence of polymer crosslinking on the mechanical properties of polydimethylsiloxane-based intrauterine systems

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## Introduction

Polydimethylsiloxane (PDMS) is used in long-acting levonorgestrel intrauterine systems (LNG-IUSs) such as Mirena® (a complex drug-device combination product intended for contraception over a period of 6 years).

LNG-IUSs consist of a drug-reservoir formed by curing the PDMS elastomer base with a crosslinking agent in the presence of LNG, an outer PDMS membrane and a polyethylene stem which is mounted with the reservoir.

The mechanical properties (hardness, elasticity and moldability) of the drug-polymer reservoir are important to retain its shape and characteristics when assembled and during insertion into the uterine cavity.

The degree and mechanism of PDMS crosslinking in LNG-IUSs may have an impact on its mechanical properties.

## Methods

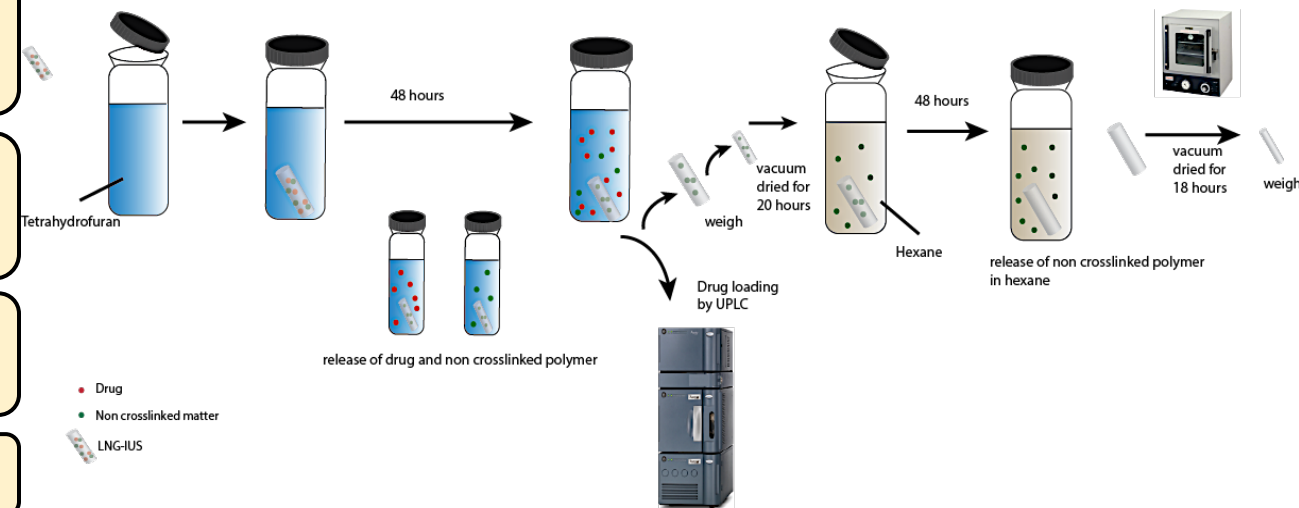
Nine different LNG-IUS drug reservoirs with 50% w/w LNG were prepared by mixing various ratios of PDMS prepolymers A and B (MED 4840 Nusil®) using a twin syringe method in a custom designed mold, followed by curing at 80°C for 24 hours.

A solvent swelling method (Fig. 1) using tetrahydrofuran and hexane was developed to determine the degree of crosslinking in the PDMS-drug reservoirs.

Drug loading and content uniformity of the drug reservoirs was ensured by a chromatographic method using UPLC.

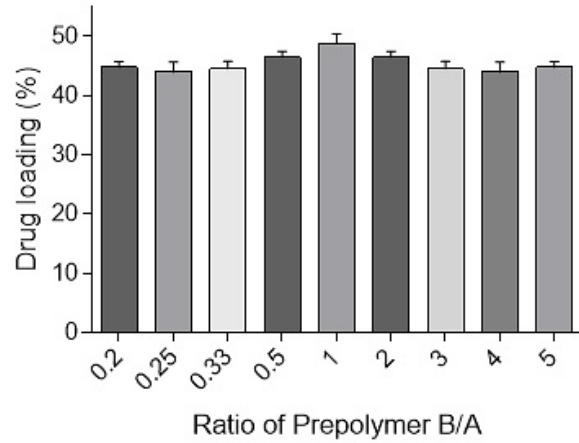
The degree of crosslinking (%) was calculated from the amount of non-crosslinked monomers extracted.

Mechanical characterization was performed using a Type-A Durometer hardness tester (Rex Gauge) and a TA.XT Plus texture analyzer (Texture Technologies Corp).

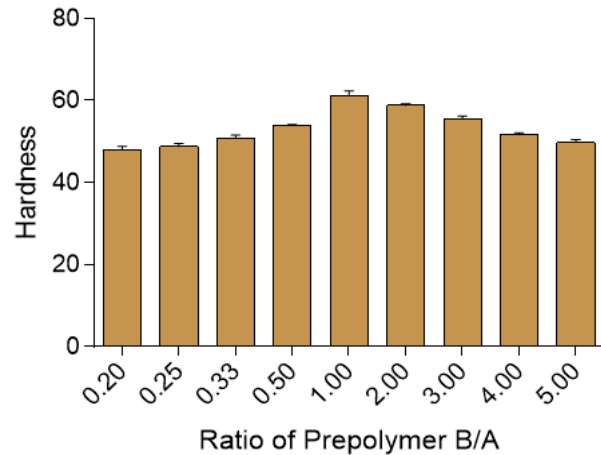


**Fig. 1.** Demonstration of the solvent swelling and extraction method to determine the polymer crosslinking in LNG-IUSs

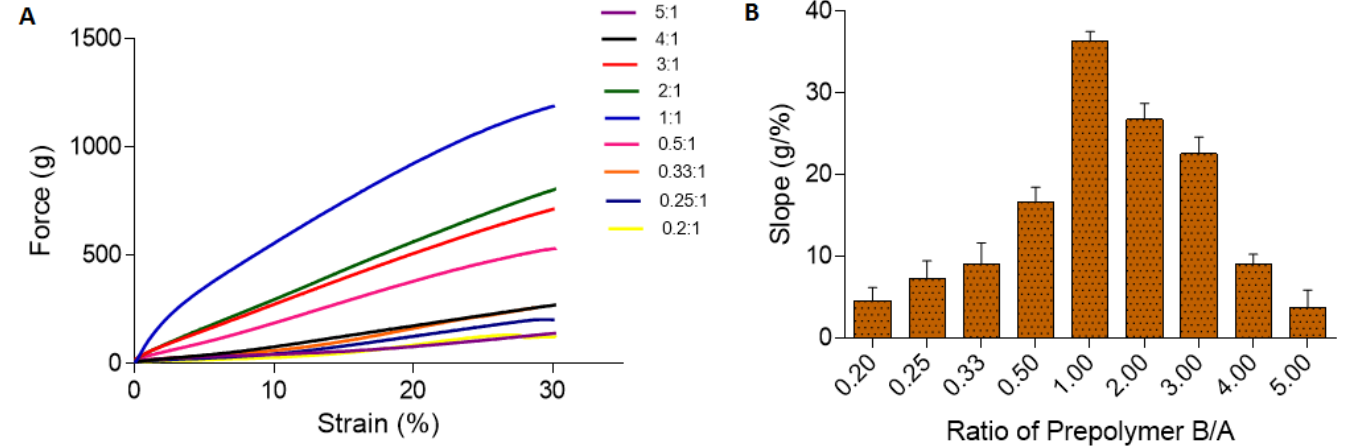
# Results



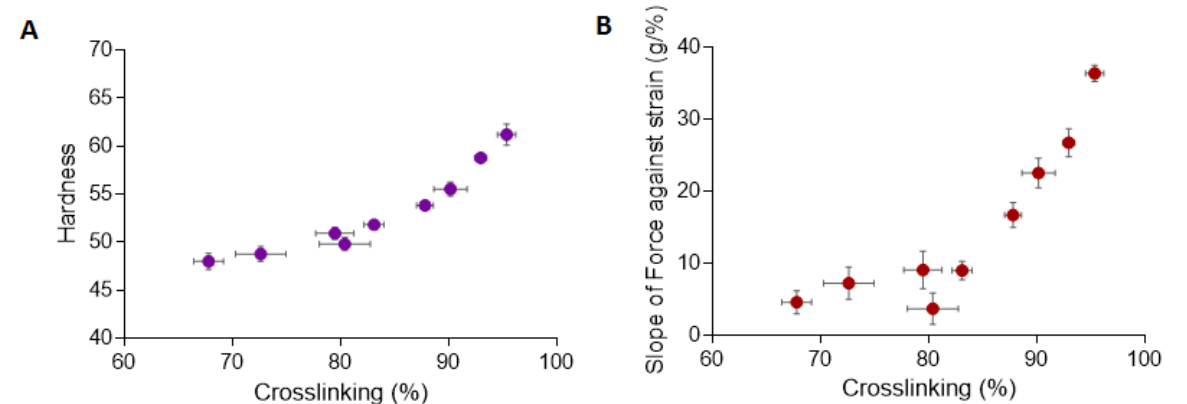
**Fig. 2.** The drug loading of different drug-polymer reservoirs prepared with 50% w/w LNG using different ratios of prepolymer A and prepolymer B (mean  $\pm$  SD, n=3)



**Fig. 3.** Hardness of LNG-IUSs with different ratios of prepolymer B/A tested using a Type-A durometer hardness tester (mean  $\pm$  SD, n=5)



**Fig. 4. A)** Plot of force against strain for LNG-IUSs prepared using different ratios of prepolymer B/A (mean, n=3); and **B)** Plot of slope (force(g)/strain(%)) and ratios of prepolymer B/A used in LNG-IUSs (mean  $\pm$  SD, n=3)



**Fig. 5.** Relationship between mechanical properties of LNG-IUSs and the degree of crosslinking: **(A)** Durometer hardness against the degree of crosslinking; and **(B)** Slope (force vs strain, using a TAXT. Plus texture analyzer) against the degree of crosslinking

## Conclusions

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- The mechanical properties of LNG-IUSs are very critical during the manufacturing, device assembly, and administration of these drug products into the uterine cavity. Currently, no standardized testing methods are available for the characterization of mechanical properties of these drug products. The current study provides the first report to characterize the mechanical properties of LNG-IUSs.
- The ratio of prepolymers significantly impacted the degree of crosslinking of the silicone elastomer, which influenced the physicochemical and mechanical characteristics of the drug reservoir. Accordingly, controlling the degree of crosslinking allows tuning of the mechanical properties of PDMS for the intended application.

## Acknowledgements

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## References

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1. Bao Q., *et al.* Manufacturing and characterization of long-acting levonorgestrel intrauterine systems. *Int. J. Pharm.*, 2018. 550, 447-454.
2. Bao Q., *et al.* Drug release testing of long-acting intrauterine systems. *J. Control. release.*, 2019. 316, 349-358.