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Zhao, X., Boyd, P., Dallal Bashi, Y., McCoy, C. F., Shen, X., Lamb, D., Kumar, N., Singer, P., Mitchell, L., & Malcolm, K. (2023). *A multipurpose 'CZL' vaginal ring for non-hormonal contraception and STI/HIV prevention*. Poster session presented at 2023 National Contraception Meeting, Houston, United States.

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# A Multipurpose 'CZL' Vaginal Ring for Non-hormonal Contraception and STI/HIV Prevention



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## Background

Marketed contraceptive vaginal rings (VR) rely upon sustained/controlled release of either a progestin (e.g., Progering<sup>®</sup>) or a progestin/estrogen combination (e.g., NuvaRing<sup>®</sup>, Annovera<sup>®</sup>). Here we report formulation development and testing of a new non-hormonal multipurpose VR incorporating three actives – copper sulphate anhydrous (CSA), zinc lactate anhydrous (ZLA), and lactide (L; hydrolyses to lactic acid, LA) (*aka*. 'CZL' ring) – and offering spermicidal, antibacterial and antiviral activity.

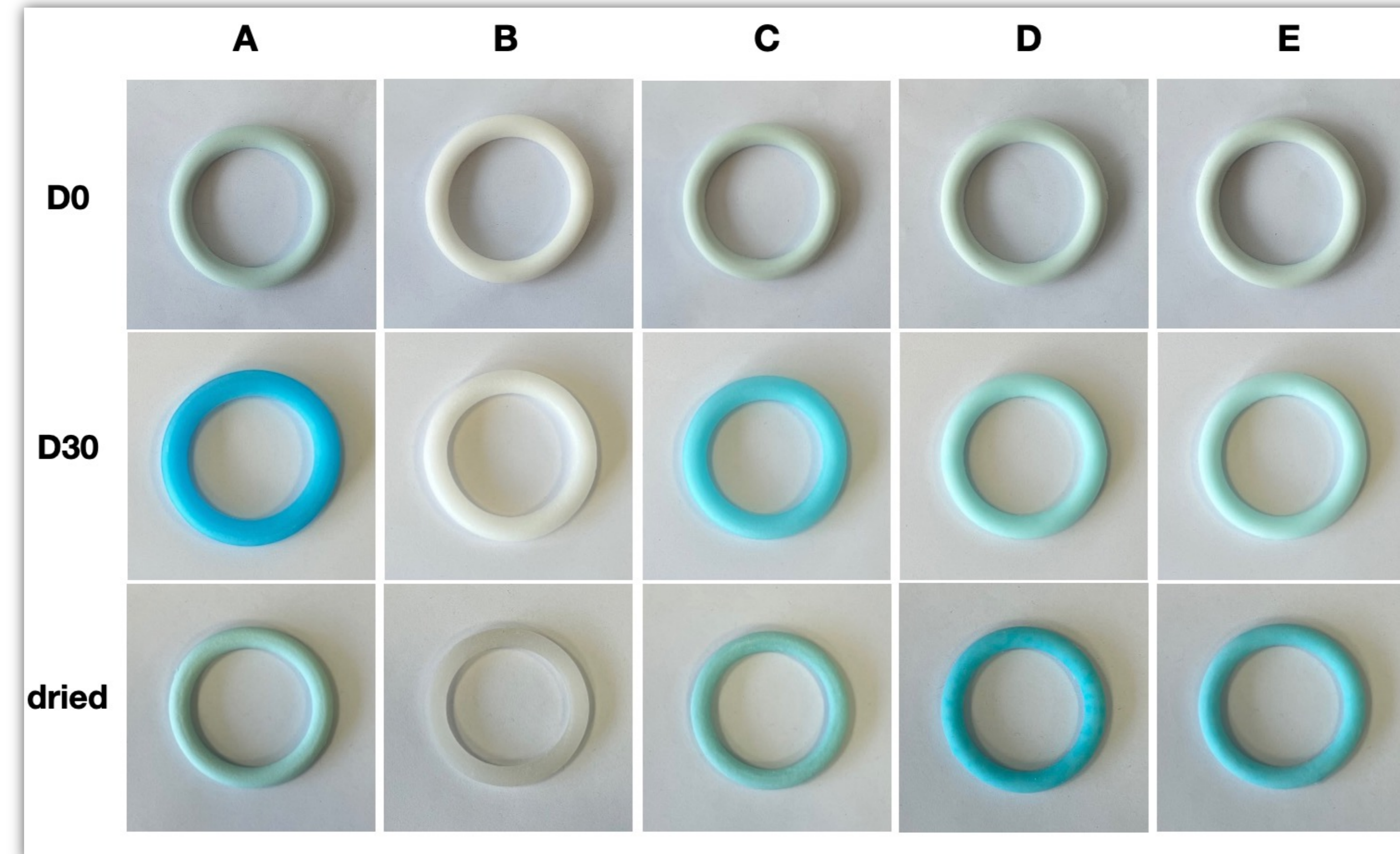
## Key points

- All VR formulations – 30% w/w CSA (30CSA), 30% w/w L (30L), 10% w/w CSA + 20% w/w L (10CSA-20L), 10% w/w CSA + 10% w/w ZLA + 10% w/w L (10CSA-10ZLA-10L), and 10% w/w CSA + 10% w/w ZLA + 20% w/w L (10CSA-10ZLA-20L) were successfully manufactured.
- The dimension of five VR formulations is ~57.4 x ~7.3 mm, and the weight varied with type within 7.8–9.3 g.
- The actives were not impacted by the VR manufacturing process, as evidenced by DSC and TGA data.
- Mechanical properties similar to marketed VR products (20 mm compression force, Shore M hardness values and percentage of elongation at break ranged 0.8–4.3 N, 41–67, 248%–564% respectively).
- Sustained and continuous release of copper and zinc ions (2–31 and 1–17 mg/day) and lactide/lactic acid (12–105 mg/day) was observed for all VRs over 30 days; these values are considered in the ballpark for clinical efficacy based on *in vitro* sperm motility/antibacterial/antiviral data (see other poster).
- VRs containing lactide maintained pH of the release medium within the range 2.2–4.6, consistent with (i) release of lactide and rapid hydrolysis to lactic acid and (ii) the pH modulating effects associated with CSA and ZLA.
- The data support the continued development of the multipurpose CZL VR concept.

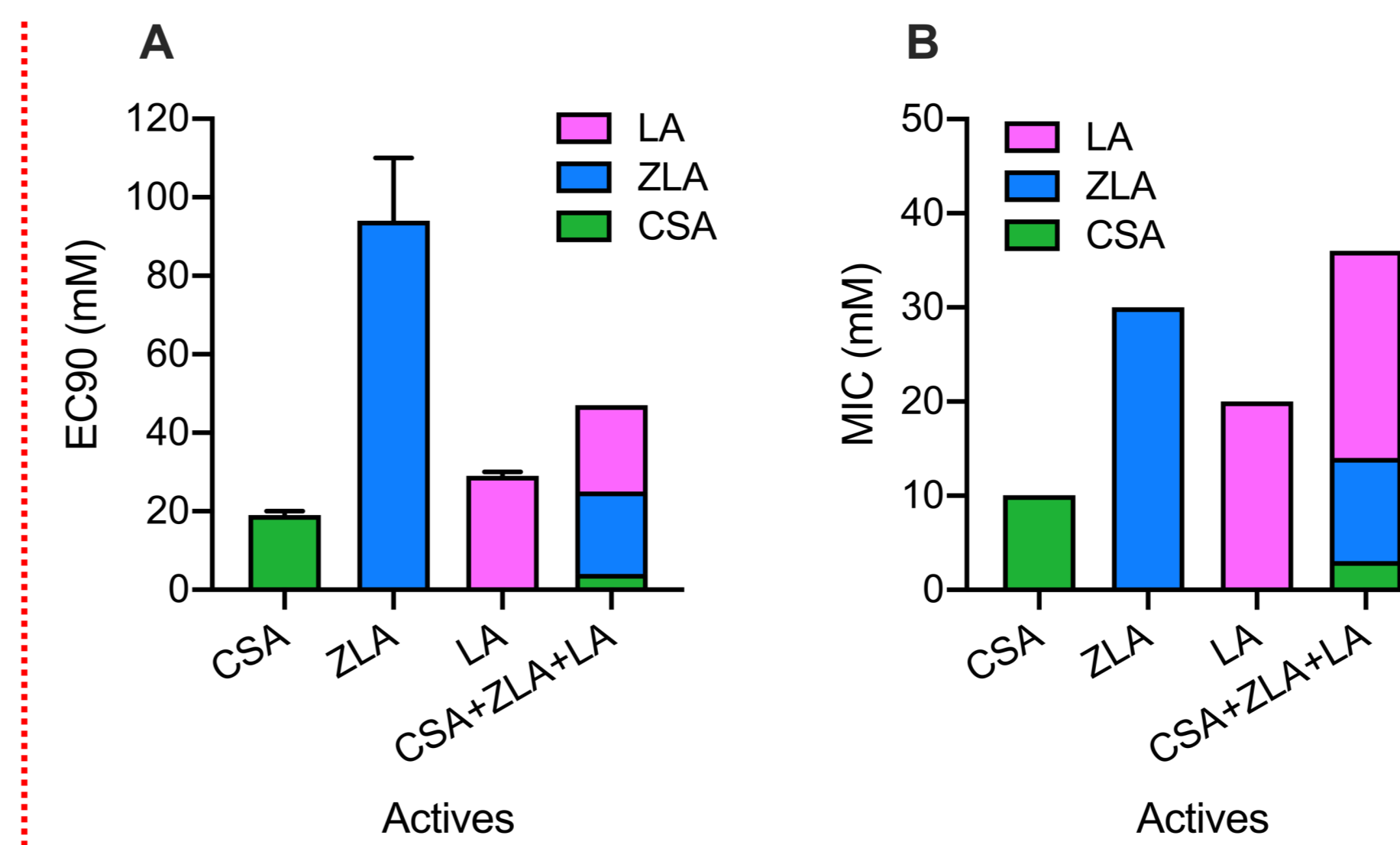
## Acknowledgements

The work was supported by NIH grant 5P50HD106793-02 ('Contraception development research center to advance a novel intravaginal ring as a non-hormonal multipurpose prevention technology').

## Results

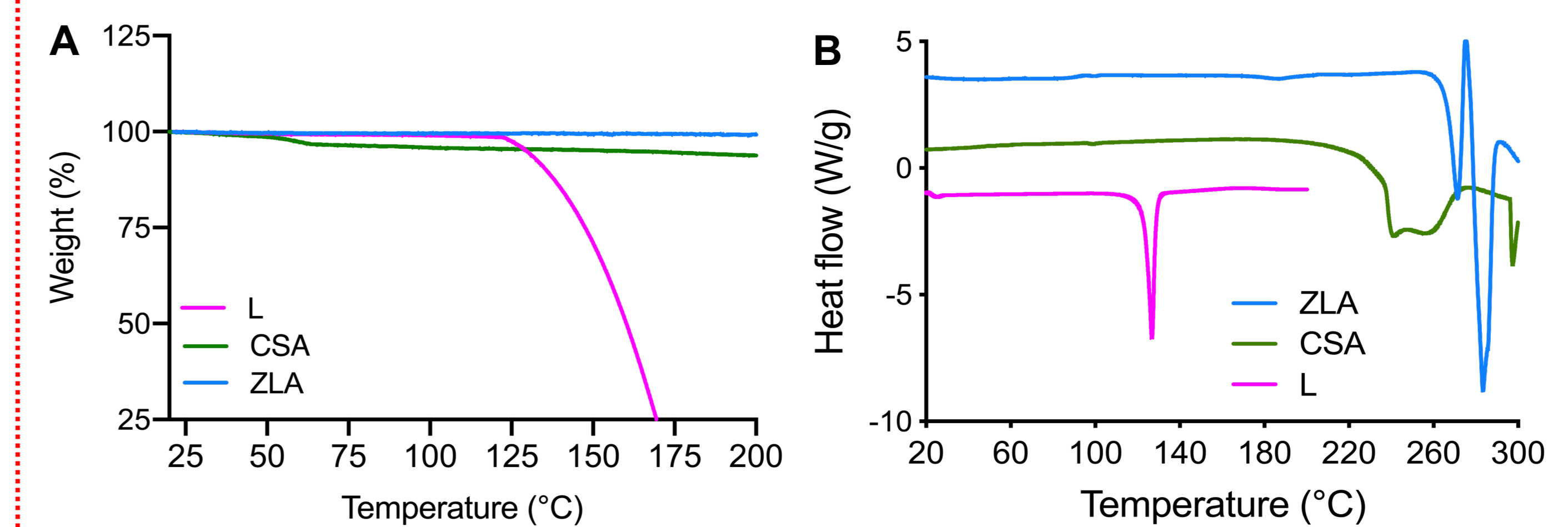


**Figure 1.** Images of matrix-type LSR4350 silicone elastomer VRs – 30CSA (A), 30L (B), 10CSA-20L (C), 10CSA-10ZLA-10L (D), and 10CSA-10ZLA-20L (E) manufactured at 115°C for 3 mins at D0 (before IVRT), after 30-day IVRT (D30) and after drying at 50 °C following IVRT (dried).

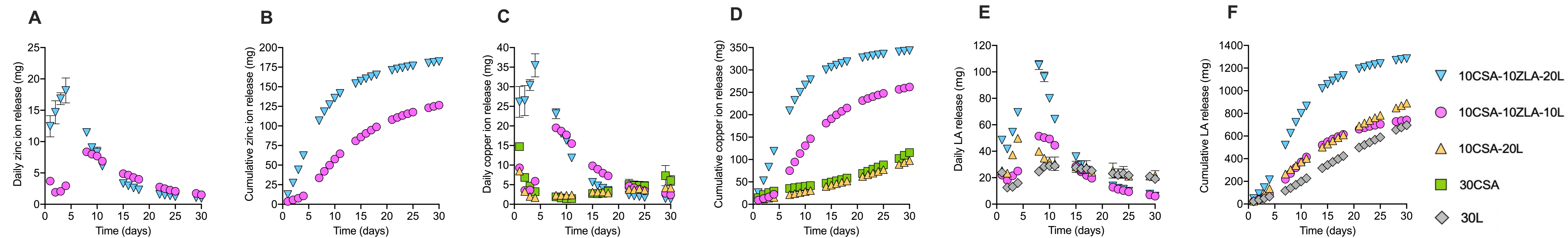


**Figure 2.** Inhibition of sperm motility test for the actives – copper sulfate anhydrous (CSA), zinc lactate anhydrous (ZLA), lactic acid (LA) only and the combination of CSA, ZLA and LA.

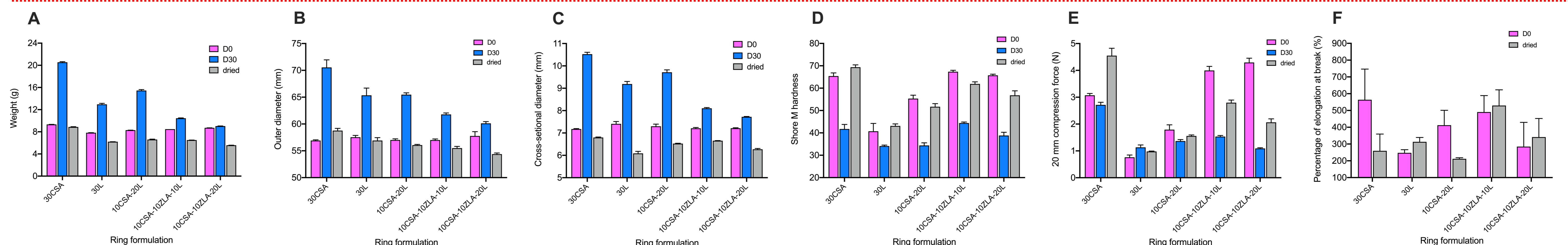
\*Minimum Inhibitory Concentration (MIC) is defined as the concentration required to inhibit progressive sperm motility.  
\*\*For 3API combos, EC90 could not be calculated empirically, and instead the smallest tested combination achieving 90% inhibition was selected.



**Figure 3.** Thermogravimetric analysis (TGA) (A) and Differential scanning calorimetry (DSC) analysis (B) for actives – zinc lactate anhydrous (ZLA), copper sulfate anhydrous (CSA) and DL-lactide (L).



**Figure 4.** Daily release of zinc ions (A), cumulative release of zinc ions (B), daily release of copper ions (C) cumulative release of copper ions (D), daily release of lactic acid (E) and cumulative release of lactic acid (F) into deionized water (60 rpm, 37°C) over 30 days.



**Figure 5.** Weight (A), outer diameter (OD) (B), cross-sectional diameter (CSD) (C), Shore M hardness (D), compression resistance at 20-mm compressive strain (E) and percentage of elongation at break in tensile testing (F) for VR formulations before IVRT (D0), after 30-day IVRT in deionised water (D30) and after 21-day drying at 50 °C following IVRT (dried).