Supplementary Information

Thermoresponsive Hydrogels for Controlled Drug Delivery to the Back of the Eye: A Data-Driven Guide to Formulation Design

Alexa K. Beathard-Wojan [a] and Vibhuti Agrahari [a*]

[a] *University of Oklahoma Health Campus, Department of Pharmaceutical Sciences, 1110 N Stonewall Ave, Oklahoma City, OK 73117, United States*

*Email: Vibhuti-Agrahari@ouhsc.edu

ORCID: Alexa K Beathard: 0009-0001-5213-1542

ORCID: Vibhuti Agrahari: 0000-0003-1884-1644

Table S1. Risk of Bias Assessment Descriptors		
Type of Bias and Description	**Manual Assessment Criteria**	**SciSpace Prompt**
Performance bias: Adherence to the study protocol. Study methods should be clearly reported and followed to ensure reproducibility.	**Low:** The authors clearly describe the experiments performed, the equipment used for measurements, and the specific conditions under which the experiments were conducted. The sources of all reagents are clearly stated. **Medium:** Study design seems logical and appropriate for the intended determinations. Proper controls are used, but descriptions are not clear enough to guarantee study reproducibility. **High:** Methods either are not appropriate or are not clear enough to determine rigor/reproducibility.	Assess the rigor of the described materials and methods section for performance bias. Where the bias is assigned low, medium, or high.
Detection bias: Validated experimental techniques are used to ensure accuracy and reproducibility of obtained results.	**Low:** The detection methods used are adequately described and appropriate for the study's objectives. **Medium:** Detection methods are vaguely described but seem appropriate for the objective. **High:** Detection methods are not described and/or are not appropriate for intended purpose.	Assess the rigor of the equipment used for detection bias to ensure validated experimental techniques are used to ensure accuracy and reproducibility of obtained results. Where the bias is assigned low, medium, or high.
Measurement Bias: When data or information is not	**Low:** The obtained data is clearly reported in the context of relevant controls, and interpretation of data is rational.	Assess the measurement Bias which measures the validity and rigor of data collection

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accurately recorded in a research study. This can stem from errors in data collection, inconsistent measurement tools, or subjective interpretation of data, leading to skewed and unreliable results.	**Medium:** Data analysis seems to make sense, but the entirety of the data collection and analysis isn't reported so rigor cannot be guaranteed. **High:** Data isn't analyzed or reported properly. Concerns related to reliability of data exist.	and reports. High levels of bias can stem from errors in data collection, inconsistent measurement tools, or subjective interpretation of data, leading to skewed and unreliable results. Assign bias as high, medium, or low.
Confirmation Bias: Conclusion support initial hypothesis without convincing experimental evidence.	**Low:** All conclusions are supported by experimental evidence. **Medium:** Conclusions are supported by evidence but seem ambitious given the reported data. **High:** Conclusions are not supported by reported data.	Assess the confirmation bias which assesses the conclusions made and if they are supported by experiments performed. High levels of bias may support initial hypothesis without convincing experimental evidence. Assign bias as high, medium, or low.

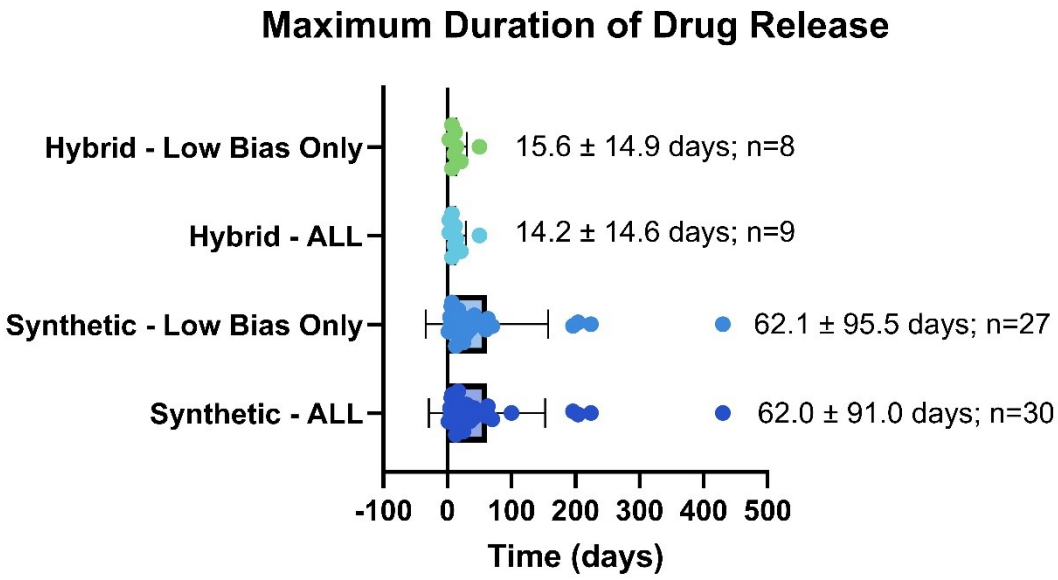

Figure S1. Maximum duration of drug release for hybrid and synthetic polymer classes across all included studies and after exclusion of studies with medium to high risk of bias in any assessed domain. Values are presented as mean ± standard deviation.

Table S2. Formulations used for percent release over time.		
Study ID	Drug used for cumulative release extraction. Note: if release was only 1 drug reported then left blank.	Formulation used for cumulative release extraction. Note: if release was only reported for 1 formulation reported then left blank.
Bakhrushina et al. (2023)	normal drug	C2
Bakhrushina et al. (2023)	solid dispersion of drug	C4
Awwad et al. (2019)		
Jiang et al. (2025)	ranibizumab in PBS (not SVF)	
Jiang et al. (2025)	rapamycin-loaded microemulsion in PBS (not SVF)	
Taheri et al. (2022)	bevacizumab	
Taheri et al. (2022)	bevacizumab in NPs	
Taheri et al. (2022)	dexamethasone	
Su et al. (2023)	Rhein	
Su et al. (2023)	Baicalein	
Wang et al. (2018)		
Xiong et al. (2018)		
Delplace et al. (2019)		unmodified HAMC
Delplace et al. (2019)		Peptide modified HAMC
Liu et al. (2024)	borneol-decorated paeoniflorin	
Liu et al. (2024)	tetramethylpyrazine	
Egbu et al. (2018)		PEGDA Hydrogel
Ilochonwu et al. (2023)	dexamethasone	10%
Ilochonwu et al. (2023)	anti-VEGF antibody fragment (biosimilar to ranibizumab)	3%
Awwad et al. (2018)	bevacizumab	8uL injection
Awwad et al. (2018)	fab-10 protein	PK eye apparatus
Pachis et al. (2017)	normal drug	18%
Pachis et al. (2017)	Liposome drug	18%
Annala et al. (2023)		
Wang et al. (2024)	ciliary neurotrophic factor	
Wang et al. (2024)	triamcinolone acetonide	
Rudeen et al. (2022)	Aflibercept	
Rudeen et al. (2022)	Dexamethasone	
Sapino et al. (2019)		Test tube release experiment
Liu et al. (2019)		2 mM, 20 mg/mL

Osswald et al. (2016)	Ranibizumab	
Osswald et al. (2016)	Aflibercept	
Xie et al. (2015)		0.625% drug load
Wang et al. (2012)		
duToit et al. (2021)		NP/PEG-PCL-PEG/PLU
Aragon-Navas et al. (2024)		PPP-T
Aragon-Navas et al. (2024)		PPP-M
Xue et al. (2019)	BSA	
Xue et al. (2019)	Aflibercept	
Xue et al. (2019)	Bevacizumab	
Lopez-Cano et al. (2021)	Dex alone	
Lopez-Cano et al. (2021)	Ketorolac alone	
Famili et al. (2014)	Normal Drug	
Famili et al. (2014)	Drug micelles	
Zou et al. (2019)		PNM1
Zhang et al. (2015)		Mixture 1; 4 mg/mL
Huang et al. (2023)	berberine	
Huang et al. (2023)	Dexamethasone	
Prosperi-Porta et al. (2017)		13/8-30
Prosperi-Porta et al. (2017)		17/6-5

*Formulation designations correlate directly to those reported in associated publications.