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A dataset on formulation parameters and characteristics of drug-loaded PLGA microparticles

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Polymer microparticles (MPs) are widely used to create long-acting injectable formulations due to their ability to enable sustained drug release. This feature can significantly benefit chronic disease management by reducing dosing frequency and improving patient adherence. To support the design and development of polymer MPs, we have compiled a dataset on MPs formed from poly(lactide-*co*-glycolide) (PLGA), the most commonly used polymer in commercial MP drug products. This dataset, derived from the literature, covers 321 *in vitro* release studies involving 89 different drugs. It aims to streamline future MP development by providing a reference for the current PLGA MP design space and supporting data-driven approaches such as machine learning. Published with open access, this dataset encourages broad utilization and aims to expand the range of available MP formulations.

Background & Summary

Polymer microparticles (MPs) are a type of long-acting injectable (LAI) formulation designed for the extended release of therapeutic agents[1–3]. Their extended-release characteristic offers substantial advantages, including improved drug pharmacokinetics[4] and enhanced patient compliance[5], which are particularly beneficial for managing chronic diseases[6,7]. Among the various polymers, poly(lactide-*co*-glycolide) (PLGA) has established itself as the gold standard material used for polymer MP formulations[8]. This preference is attributed to PLGA's biocompatibility[9], tunability[10], and biodegradability[11]. The wide usage of PLGA is evidenced not only by the extensive research dedicated to it but also by its success in clinical trials. To date, most FDA-approved polymer MP drug products are formulated using PLGA, with examples including Lupron Depot® for the treatment of hormone-related diseases[12], Bydureon® for managing type 2 diabetes[13], and Zilretta® for alleviating osteoarthritis symptoms[14]. These commercially available PLGA MP products are engineered to provide local and/or systemic drug release, with durations ranging from one week to six months, to meet various therapeutic needs[15,16].

However, since the approval of the first PLGA MP drug (Lupron Depot®) by the FDA in 1989, only about ten PLGA MPs have been approved and reached the market[16,17]. A significant challenge in the development of these MPs is their high-dimensional formulation design space[18]. The MP development process involves navigating this design space by formulating MPs using numerous combinations of excipients and formulation parameters. These MPs are then analyzed to identify the lead candidates with desirable performance characteristics, including particle size, drug loading, and drug release profiles. However, the complexity of this design space and the time-consuming nature of pharmaceutical studies make comprehensive evaluation of all potential MPs practically impossible[19]. This limitation can lead researchers to focus on a narrow range of formulation parameters (especially those documented in the literature) to optimize MPs more efficiently. For example, the majority of the existing PLGA MP studies concentrate on PLGA with a lactide (LA) to glycolide (GA) ratio of 1:1 or 3:1 and polymer molecular weights ranging from 12 to 75 kDa (Fig. 1). However, as different therapeutic agents have unique properties, the formulations optimized for one drug might not be optimal for another. Therefore, limited exploration can lead to suboptimal formulation development and, ultimately, less desirable performance. To address this, researchers have started to integrate machine learning (ML) as a data-driven approach to examine the drug formulation design space in a more efficient manner[19,20]. ML, an important subfield of artificial intelligence, is increasingly recognized across various sectors, including chemistry, materials science, drug discovery, and recently formulation development[21,22]. However, despite substantial progress in the field, the broader

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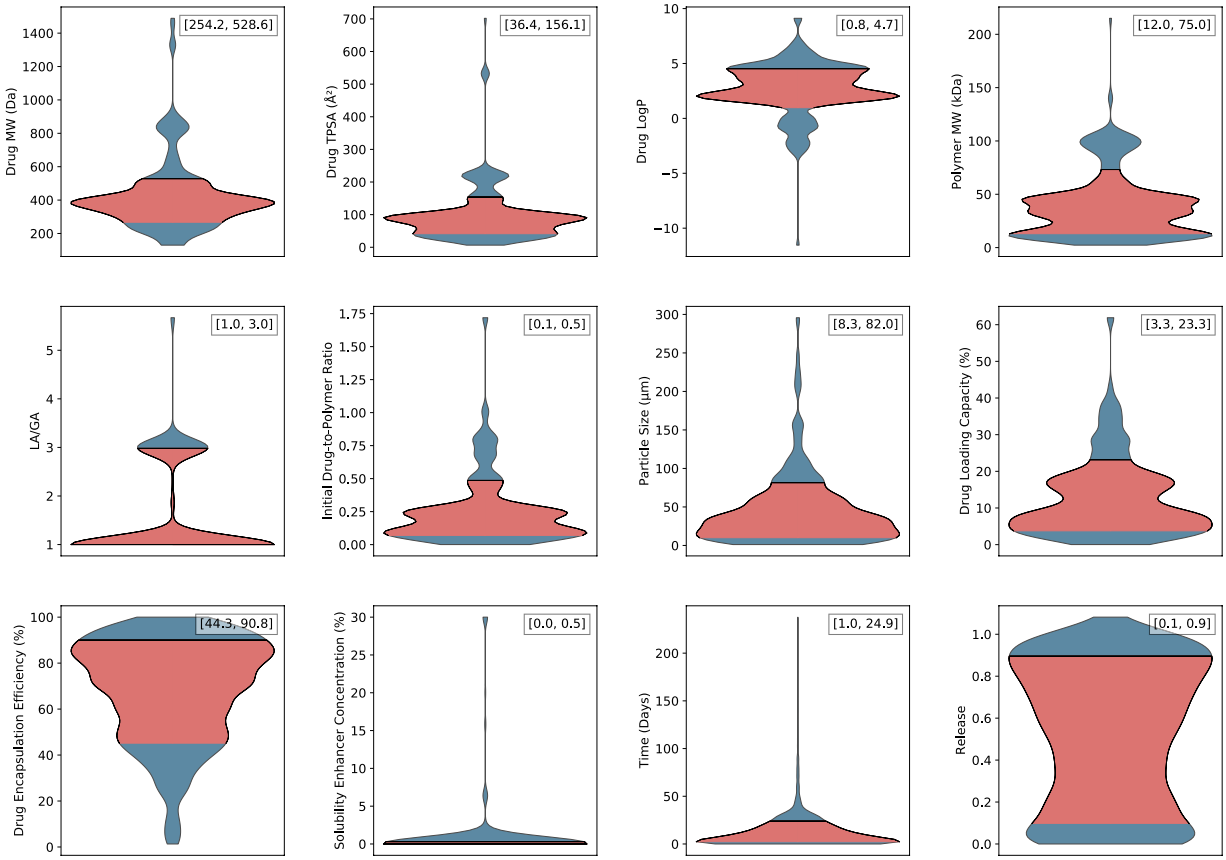

Fig. 1 Violin plots showing the distributions of the formulation descriptors in the processed dataset. The red shaded areas represent the central 70% of the data (from the 15th to the 85th percentile), while the blue areas indicate the remaining 30% of the data. The labels in the top right of each plot indicate the range of the central 70% of the data for each descriptor.

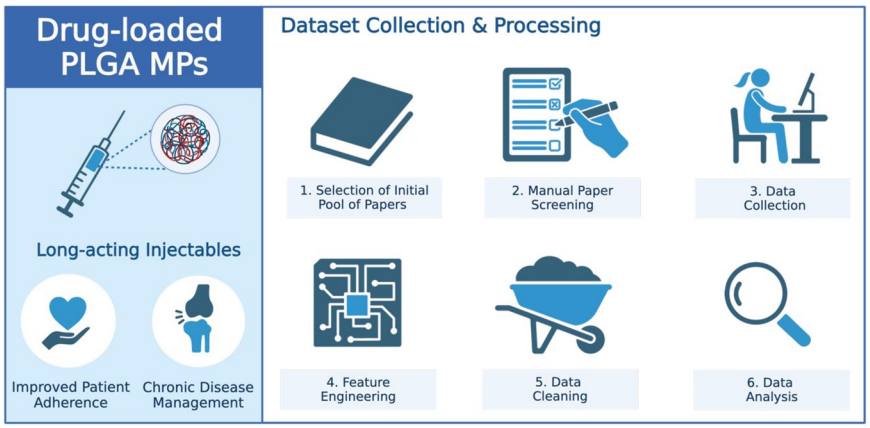

Fig. 2 Overview of the drug-loaded poly(lactide-*co*-glycolide) microparticles (PLGA MPs), and the dataset collection and processing workflow. The left section highlights the application of PLGA MPs as long-acting injectables, illustrating benefits including improved patient adherence and chronic disease management. The right section outlines the procedures for dataset collection and processing, beginning with selection of the initial pool of papers, followed by manual paper screening, data collection, feature engineering, data cleaning, and data analysis.

application of ML in pharmaceutical sciences is in part constrained by the lack of accessible datasets for model development[23].

To mitigate these challenges, this work presents a literature-mined dataset on formulation parameters and characteristics of PLGA MPs (Fig. 2). This dataset comprises 321 *in vitro* PLGA MP release experiments with 4913 *in vitro* release time points, collected from 113 publications. To the best of the authors' knowledge, this

Criteria	Go/No-Go Decision
Relevance	Is the paper relevant to the scope and objectives of the dataset (i.e., PLGA MPs for small molecule delivery)?
Completeness of Release Profile(s)	Are release profile(s) of drug(s) from PLGA MPs reported, with data spanning at least 72 hours and a final release exceeding 60%?
Formulation Method Completeness of Data and Information	Are the PLGA MPs prepared using an emulsion-based method? Are all necessary data points and experimental details clearly reported and available in the manuscript?

Table 1. Criteria for paper selection for curation of dataset.

Descriptor	Unit	Dataset Presence	Description
Formulation Index	n/a	Both	List of *in vitro* release experiments in the dataset.
Drug	n/a	Initial	Name of the drug loaded into the PLGA MPs.
Drug SMILES	n/a	Initial	SMILES string of the drug loaded into the PLGA MPs.
Polymer Mw	kDa	Initial	Weight average molecular weight of the PLGA used for MP preparation.
Polymer Mn	kDa	Initial	Number average molecular weight of the PLGA used for MP preparation.
Polymer Molecular Weight (unit not specified)	kDa	Initial	Molecular weight (unit not specified) of the PLGA used for MP preparation.
Polymer MW	kDa	Processed	PLGA molecular weight (Mw, Mn, or unit not specified, depending on availability) used for data visualization.
PDI	n/a	Initial	Polydispersity index of the PLGA used for MP preparation.
LA/GA	n/a	Both	Molar ratio of lactide to glycolide repeat units in the PLGA polymer.
Formulation Method	n/a	Initial	Type of formulation method used for PLGA MP preparation.
Initial Drug-to-Polymer Ratio	w/w	Both	Weight ratio of the initial drug to PLGA used for MP formulation.
Particle Size	μm	Both	Diameter of the PLGA MPs.
Drug Loading Capacity	%	Both	Weight percentage of the drug encapsulated relative to the drug loaded PLGA MPs.
Drug Encapsulation Efficiency	%	Both	Weight percentage of the drug encapsulated relative to the initial total drug used for formulation.
Solubility Enhancer Concentration	%	Both	Concentration of the solubility enhancer used in the *in vitro* release media.
Time	Day	Both	Time at which a specific release sample was taken.
Release	w/w	Both	Fractional drug release from the PLGA MPs over time.
DOI	n/a	Initial	DOI of the papers from which the data was collected.
Drug MW	Da	Processed	Molecular weight of the drug.
Drug TPSA	Å²	Processed	TPSA of the drug.
Drug LogP	n/a	Processed	LogP of the drug.

Table 2. Overview of the formulation descriptors in the initial and/or processed datasets. Drug SMILES strings were primarily collected from the Chemical Abstracts Service database, and from PubChem when not available. When any of the initial drug-to-polymer ratio, drug loading capacity, or drug encapsulation values were missing, they were calculated using the other two parameters, if possible. Drug MW, TPSA, and LogP were computed using 'RDKit' based on the drug SMILES strings. When both polymer Mw and Mn were available, Mw was used for visualization due to its prominence and widespread use as reported in the literature. In cases where neither Mw nor Mn was available, the Polymer Molecular Weight (unit not specified) was used for visualization.

dataset is the most extensive, open-access dataset available on drug-loaded PLGA MPs. This dataset is expected to streamline future MP design by providing a reference for the current formulation design space and serving as a readily accessible resource for ML model development. By offering open access to this data, we aim to facilitate its broader use by the community and establish a foundation for future work to include other polymers and dosage forms.

Methods

Data collection. For this dataset, PLGA MP studies were sourced from the Web of Science database using the keywords: "PLGA microparticles/microspheres" and "drug delivery". Given the dataset's focus on drug-loaded PLGA MPs, the search was further refined by excluding terms including "proteins," "peptides," "nanoparticles," and "nanospheres," and limited to research articles only. This process yielded an initial pool of 1231 articles. Each paper was manually reviewed to verify its relevance, completeness of *in vitro* release profiles, and the presence of all information used as formulation descriptors prior to data collection. Specifically, release data were required to span at least 72 hours with a final reported release exceeding 60%. This was to ensure the long-acting nature of the MPs and at least near to complete release of the drug. Additionally, the method of preparation of the formulation was restricted to the emulsion method, chosen for its widespread use and data availability. These paper selection criteria are summarized in Table 1.

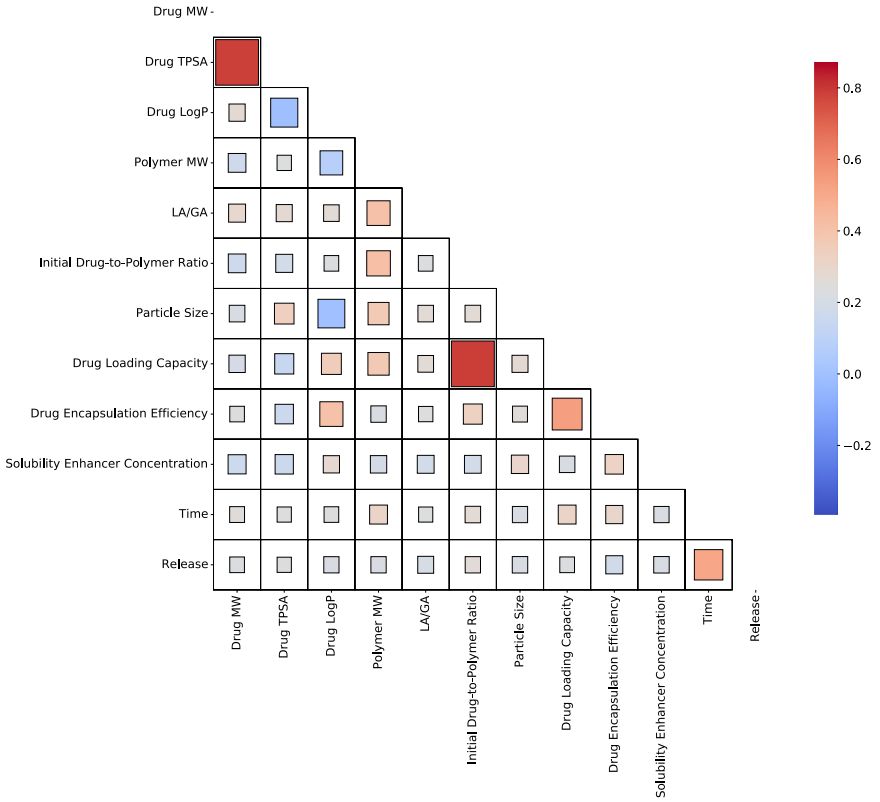

Fig. 3 This figure illustrates a correlation matrix demonstrating the pairwise Pearson correlations among all descriptors in the processed dataset. The intensity of the color and the size of each square represent the magnitude of the correlation. Aside from time, formulation features exhibit low Pearson correlations with drug release, suggesting that their relationships with drug release are likely complex, multidimensional, and non-linear.

After manual screening, 113 papers were identified[24–136]. From these, relevant descriptors (Table 2) were collected from the original publications. Specifically, drug release data were extracted from reported release profiles using the WebPlotDigitizer (Version 4). Furthermore, the simplified molecular input line entry system (SMILES) strings of the drugs were collected from the Chemical Abstracts Service (CAS) and PubChem databases for further feature engineering. The abbreviations and definitions of all descriptors are summarized in Table 2.

Feature engineering and data cleaning. To prepare this dataset for data analysis and future use in ML, further feature engineering and data cleaning were performed. First, three drug descriptors including molecular weight, topological polar surface area (TPSA), and LogP were added. These descriptors were computed using the '***RDKit***' library, based on the drug structures represented by their SMILES strings. Definitions of these descriptors are summarized in Table 2. Subsequently, non-numerical descriptors were then removed from the dataset prior to data analysis.

Dataset feature distribution analysis. The distribution of the features in the processed dataset was visualized using violin plots created with '***seaborn.violinplot***' (Fig. 1). The central 70% of the data, ranging from the 15th to the 85th percentiles, is colored in red to highlight the central tendency and narrow spread of the majority of the data points. The range of this 70% was indicated in the top left of each subplot. The remaining 30% data is colored in blue.

Dataset feature correlation analysis. To analyze the correlation between features in the processed dataset, Pearson correlation coefficients (PCCs) were computed using the '***pandas.DataFrame.corr***' and visualized in a heatmap with the '***seaborn***' and '***matplotlib***' packages (Fig. 3). PCCs between features were represented by the colors of squares, with deep blue indicating strong negative correlations and deep red indicating strong positive correlations. To enhance clarity, the strength of the correlations was also depicted by the size of the squares, with stronger correlations represented by larger squares, and vice versa.

File	Description
mp_dataset_all_papers.xlsx	This file contains a list of all papers included in the initial pool.
mp_dataset_initial.xlsx	This file contains the collected PLGA MP formulations, along with their descriptors sourced from original studies and the CAS/PubChem databases.
mp_dataset_initial_formulation.xlsx	This file contains the same data as the mp_dataset_initial.xlsx, but duplicates resulting from evaluation of the same formulation at multiple time points have been removed to simplify indexing.
mp_dataset_processed.xlsx	This file contains the processed PLGA MP dataset after feature engineering and cleaning.
mp_dataset_feature_engineering_cleaning.ipynb	This file contains the Python code used for dataset feature engineering and data cleaning.
mp_dataset_data_analysis.ipynb	This file contains the Python code used for data analysis (i.e., distribution, correlation and visualization.

Table 3. Overview of datasets and associated files with descriptions.

Data Records

The PLGA MP dataset, along with other relevant files, is available as open-access via Mendeley Data (https://data.mendeley.com/datasets/zzvtdrcy76/2)[137]. These files include the (1) original list of all papers before screening, (2) the initial dataset, (3) the initial dataset refined for indexing, (4) the processed dataset, (5) the Python codes used for feature engineering and data cleaning, and (6) the Python codes used for data analysis and visualization. A detailed overview of these files is provided in Table 3. In total, the final processed dataset contains 321 *in vitro* PLGA MP release experiments, with a total of 4913 release points.

Technical Validation

The dataset presented in this paper is derived from PLGA MP formulations reported in the literature, and its quality is directly related to the original studies. To minimize manual bias during paper screening and data collection, a dual review process was employed. Specifically, two authors independently screened all papers and collected data to reduce potential errors in data collection and input. Any discrepancies were resolved through the discussions between the two authors, or if necessary, by consulting a third author. Furthermore, to ensure the dataset's utility for ML applications, its standardization and completeness have been verified. First, all units reported from different studies were standardized to commonly used units, including polymer molecular weight in kilodaltons (kDa), release sampling timepoints in days, and drug release in fractional values. In addition, the dataset (mp_dataset_processed.xlsx) was checked to ensure the availability of all descriptors, eliminating the need for additional procedures to address missing data prior to use.

Code availability

The Python scripts for feature engineering, data cleaning, and data analysis are available on Mendeley Data along with the datasets (https://data.mendeley.com/datasets/zzvtdrcy76/2)[137].

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Author contributions

Z.B. co-led the conceptualization of this work, led the data analysis, and wrote the first draft of the paper. J.K. and C.K. performed the literature review and data collection. F.L.D. reviewed and edited the manuscript. C.A. co-led the conceptualization of the work, led the supervision of the work, acquired research funding, and led the review/editing of the paper. All authors read and approved the final manuscript.

Competing interests

CA is a cofounder and CEO of Intrepid Labs Inc.

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