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Impact of Surface Properties — Including Pore Size — of Porous Structures on Anticancer Drug Delivery Efficiency in Colon Cancer: A Systematic Review

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Impact of Surface Properties — Including Pore Size — of Porous Structures on Anticancer Drug Delivery Efficiency in Colon Cancer: A Systematic Review

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Abstract

Porous materials with micro-, meso-, and macroporous structures receive increasing attention as multifunctional platforms for targeted drug delivery in colon cancer therapy. Their adjustable pore sizes, tunable surface chemistry, and adaptable structural frameworks enable controlled drug loading and release. Pore size distribution's impact on treatment efficacy is under-investigated.

In line with PRISMA 2020 guidelines, this review systematically examined more than 3,000 studies and, based on performance criteria, identified 203 articles for inclusion. The IUPAC pore classification elucidates the impact of pore diameters on drug diffusion, cellular uptake, and cytotoxicity, highlighting their essential function in multi-modal treatment techniques.

Recent advancements in pH-responsive systems, aptamer-mediated targeting, and hierarchical porosity engineering illustrate how these integrated mechanisms augment site-specific drug delivery and enhance therapeutic selectivity. The review emphasizes essential design principles and future outlooks for creating next-generation porous carriers, whereby pore size, surface functionality, and biological responsiveness work in concert to enhance colon cancer therapy.

1. Introduction

Porous drug-delivery platforms have become central to emerging therapeutic strategies for colon cancer due to their high surface area, tunable internal architecture, and capacity for controlled drug loading and release.[1] In the past ten years, materials such as mesoporous silica,[2] metal–organic frameworks,[3] polymeric hydrogels,[4] zeolites,[5] and hybrid nanoarchitectures[6] have demonstrated promising in-vitro performance Nonetheless, despite the variety of existing systems, a critical question persists: to what degree does pore size, independent of material chemistry, influence cytotoxic effects in colon cancer models? [7]

Most current evaluations classify porous systems according to material type or synthesis method, which complicates the assessment of mechanistic trends that transcend material categories.[8] The literature is deficient in a cohesive analytical framework based on the IUPAC pore-size classification (microporous <2 nm, mesoporous 2–50 nm, macroporous >50 nm).[9] This deficiency is significant, as pore size can influence diffusion resistance, surface interactions, steric compatibility with drug molecules, and intracellular processing pathways. In the absence of a pore-centric perspective, it is difficult to ascertain if the enhanced biological performance observed for specific carriers is due to their chemical composition, porosity, or a relationship between the two factors.

Significant variability in drug classes, release profiles, assay conditions, and colon cancer cell models further complicates the available evidence.[10] What is lacking is a systematic, cross-platform comparison that assesses porous carriers based on pore size while incorporating cytotoxicity results across diverse experimental designs.

This study does a PRISMA-aligned[11] a systematic review, including over two thousand screened records and 203 eligible studies. Our study topic is: Does pore size, classified according to the IUPAC framework, [12] independently correlate with in vitro cytotoxic efficacy in colon cancer models?

This evaluation employs a normalization-centered analytical methodology[13] to achieve suitable comparability among investigations, given the significant variability of reported IC_{50} values[14] in the literature. IC_{50} datasets were specifically processed using Box–Cox normalization[15] to mitigate skewness and stabilize variance across pore-size categories. Subsequent to transformation, Q–Q plots[16] were utilized to evaluate the degree of distributional normality attained and to confirm the appropriateness of the data for parametric statistical analysis.

A two-way ANOVA[17] was conducted on the normalized dataset to assess the independent or interactive effects of pore-size classification, according to the IUPAC framework, and the colon cancer cell model on in vitro cytotoxic performance.[18] I In this analysis, pore type and cell line were considered two separate explanatory variables. This methodology enables the investigation to ascertain both the primary influence of pore-size on IC_{50} values and the systematic variation of cytotoxic responses among cell lines, in addition to identifying any statistically significant interaction between these two variables.

A two-way ANOVA is appropriate for this analysis because the dataset includes several cell models and multiple pore-size categories, [19] both of which can influence the biological response simultaneously.[20]

The method partitions the variation into main and interaction effects, making it possible to distinguish pore-size trends from cell line–specific differences.

As a result, any observed changes in cytotoxicity can be interpreted as genuine cross-platform patterns rather than artifacts caused by the inherent heterogeneity of colon cancer model systems.

Objective

To systematically assess the impact of pore type and porous morphology on the anticancer efficacy (IC50, viability, and cytotoxicity) of porous drug-delivery devices evaluated in in vitro colon cancer models.

2.Materials and methods

2.1. Registration

This protocol has been prospectively filed in PROSPERO with the registration number CRD420251108499, dated 20 July 2025. Any further revisions will be documented in the PROSPERO registry.[21]

2.2. PICOS framework

2.2.1. Population:

In vitro models of colon cancer cells were assessed for cytotoxicity or anticancer efficacy.

2.2.2. Intervention:

Porous drug delivery systems (DDSs) featuring micro-, meso-, or macroporous structures, where the pore type was either explicitly stated or could be deduced from the morphological data presented in the article (e.g., pore size details, structural characterization, or descriptive morphological observations).[22]

2.2.3. Comparator:

The comparator could be either an unmedicated control, an inert carrier/drug delivery system, or alternative porous substances.

2.2.4. Outcomes:

Principal outcomes: IC50 values and cellular viability.
Secondary outcomes: Properties linked to surface characteristics, pore size and type, and additional morphology-dependent descriptors documented in the included research.

2.2.5. Study design:

The research methodology involved conducting original in vitro experimental investigations.

2.3. Eligibility criteria

2.3.1. Inclusion Criteria

The eligibility criteria includes conducting initial in vitro investigations on colon cancer models.
The use of porous drug delivery systems, whether micro-, meso-, or macroporous, is a requirement.
The study ensures the accessibility of IC50 values or extractable dose-response data.
The article contains adequate morphology-related information to categorize pore type, including pore-size statistics, structural properties, and descriptive morphological reporting.

2.3.2. Exclusion Criteria

The study excludes research that uses colon cancer models.
There should be no assessment of cytotoxicity or cell viability.
Impermeable systems.
The literature includes reviews, patents, books, conference abstracts, and secondary research.
Absence of extractable IC50 or inadequate morphology-related data.

2.4. Search strategy

This systematic review was performed in compliance with PRISMA 2020 principles. A comprehensive search was performed across three electronic databases—Scopus, Web of Science Core Collection, and Google Scholar—to ensure extensive coverage of materials science, chemistry, nanotechnology, and biomedical literature relevant to porous drug-delivery systems for colon cancer. The search for Scopus and Web of Science was confined to papers from 2015 to 2025, corresponding to the era when modern porous structures and contemporary drug-delivery techniques gained prominence. In Google Scholar, which indexes a broader and less organized array of sources, the

search parameters were confined to 2019–2025 to minimize irrelevant results from non-curated entries while maintaining adequate sensitivity for recent advancements.
A three-block Boolean framework was employed, utilizing language pertinent to porous materials, anticancer drug delivery, and colorectal cancers, while omitting non-original research. The fundamental Boolean query was
("hydrogel" OR "magnetic hydrogel" OR "MOF" OR "COF" OR "ZIP" OR "porous structure*" OR "pore size" OR "mesoporous silica" OR "mesoporous carbon" OR "mesoporous" OR "macroporous" OR "nanoporous" OR "zeolite" OR "diatom" OR "HAP" OR "ceramic*" OR "MSN") AND ("drug delivery" OR "anticancer drug*") AND ("colon cancer") NOT ("review" OR "thesis" OR "book" OR "patent")
Database-specific modifications were implemented as necessary, encompassing field tags, truncation protocols, and filters for dates or document types. The comprehensive search strings for Scopus, Web of Science, and Google Scholar, along with all implemented filters, are included in the Supporting Information to guarantee perfect repeatability. The date of the last search and the deduplication process are also recorded.
The selection of studies is depicted in a PRISMA 2020 flow diagram, including the quantity of retrieved records, duplicates eliminated, titles and abstracts evaluated, full texts reviewed, reasons for exclusion, and the final collection of studies incorporated in the qualitative synthesis.

2.5. Study selection

Two impartial evaluators assessed the titles and abstracts of all obtained records to ascertain possible eligibility. The complete texts of the chosen publications were thereafter examined independently to verify inclusion based on the established criteria. Discrepancies between the two reviewers' decisions were addressed through discussion and, as required, by consulting a third senior reviewer. The inter-reviewer agreement in the screening phase was measured using Cohen’s kappa coefficient to guarantee methodological reliability.

2.6. Data extraction

The data extraction occurred in two phases.
In Stage 1, information pertaining to materials—including material classification, pore category, pore morphology, and structural descriptors—was extracted. Poor categorization was estimated by two reviewers based on structural or characterization data where pore size was not explicitly stated, with consensus achieved through debate.
IC_{50} values were obtained in Stage 2. Numerical IC_{50} values were recorded directly from the investigations. In instances where the IC_{50} was not numerically specified, the dose–response curve (illustrating cell viability against concentration) was digitized utilizing WebPlotDigitizer[23] (v4.6) to ascertain the IC_{50} value. An Excel file specifically for IC_{50} extraction recorded the extraction methodology (direct, converted, or digitized), unit-standardization procedures, and method-specific annotations. Every submission was designated a quality flag to guarantee traceability and consistency among experiments.

2.7. Risk of bias assessment

The risk of bias for the included in vitro cytotoxicity studies was evaluated using a structured checklist derived from recognized quality frameworks for laboratory research, incorporating elements from QUIN,[24] SciRAP,[25] and NIH criteria for in-vitro methodology.[26]. The modified assessment tool consisted of six methodological domains:
Assay validity: suitability of the cytotoxicity or viability assay, accurate readout conditions, and application of validated techniques.
Ensure transparency: provide clarity and comprehensiveness in the reporting of biological/technical replicates and sample size.
Assessment of control adequacy: characterization and suitability of negative and positive controls employed in cytotoxicity assays.

Integrity of dose–response: clarity, completeness, and internal consistency of the dose–response assessment.
Outcome reporting for IC_{50} refers to the reliability of the inhibitory concentration values that are presented.
This reliability is usually classified into three levels.
IC_{50} values fall into the lowest concern tier when they are reported directly in common units, such as μM or μg/mL.
Reporting results in these established units is widely practiced, which contributes to their overall credibility.
IC_{50} was reported with non-standard, incomplete, or inconsistent units necessitating unit conversion: assessed as unclear concern (1) due to conversion-related ambiguity.
IC_{50} is not quantitatively stated and is derived from dose–response curves via WebPlotDigitizer (v4.6) [23]: categorized as high concern (0) due to variability dependent on digitization.
Outcome completeness: the presence of numerical data, the ability to derive curves, and the uniformity among text, figures, and supplementary resources.
Each domain was scored using a three-level scale (2 = low concern, 1 = unclear, 0 = high concern), yielding an overall quality score ranging from 0 to 12 for each study. Following laboratory-quality evaluation practices, studies were classified as:
0–4 = high risk of bias,
5–8 = unclear risk,
9–12 = low risk.
Two reviewers conducted all risk of bias evaluations independently. In studies necessitating digitization, both reviewers separately extracted IC_{50} values from dose–response plots via WebPlotDigitizer, [23] and disagreements were reconciled through discussion to reduce extraction-related errors. Inter-reviewer agreement was assessed using Cohen's kappa, with kappa values and domain-level scoring summaries provided in the Supporting Information.

2.8. Statistical analysis

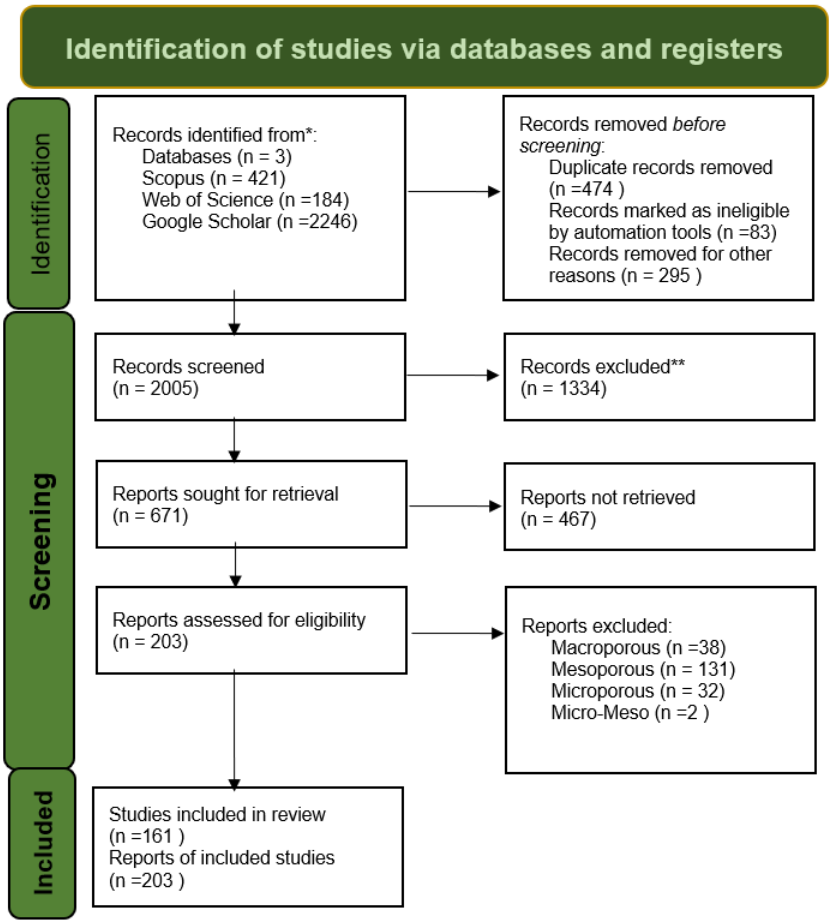
IC_{50} values were descriptively summarized within each pore size category utilizing measures of central tendency and dispersion, including median, interquartile range, range, standard deviation, and coefficient of variation. [27] To mitigate skewness and stabilize variance across studies, IC_{50} values were transformed via the Box-Cox procedure prior to inferential analysis.
Due to significant clinical and methodological heterogeneity among trials, no quantitative meta-analysis (no aggregated effect size) was conducted. [15] A two-way analysis of variance (ANOVA) [28] was employed on Box–Cox–transformed IC_{50} values to evaluate the primary impacts of cell line and pore-size category, together with their interaction (Cell × Pore Type). Statistical significance was established at $p < 0.05$. Polynomial curve fitting was utilized solely as a descriptive instrument and was not employed for formal hypothesis testing.
All statistical analyses (Box–Cox transformation,[15] two-way ANOVA,[28] post-hoc tests) and machine-learning models[29] (Linear Regression,[30] Random Forest, [31] XGBoost ,[32] SVR, [33] Gaussian Process, [34] MLP, [35] UMAP, [36] t-SNE, [37] Kernel PCA ,[38] SOM, [37] and GMM [37]) were implemented in Python (v3.10).[39]

3.Results

3.1 Overview of dataset

A total of 203 studies met the inclusion criteria and were categorized using the IUPAC pore-size framework.
Within this group, 131 systems were identified as mesoporous, 38 as macroporous, 32 as microporous, and 2 as micro–mesoporous hybrids.
These studies cover a broad range of porous materials applied in colon cancer models, including including MOFs, [40] COFs, [41] hydrogels, [42] zeolites, [43] nanocellulose, [44] micelles, [45] and polymeric hybrids.[46]
Each material type presents distinct structural features and corresponding drug-release behavior.

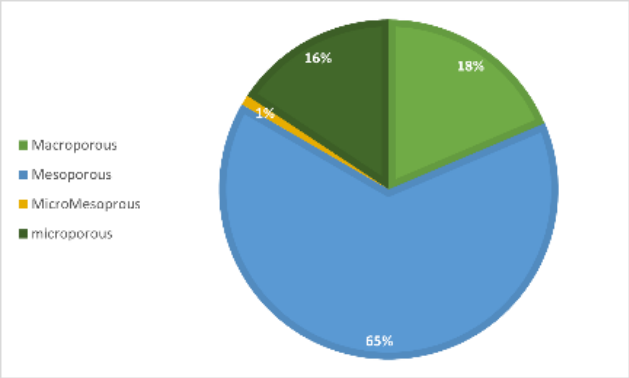
Figure 1.PRISMA flow diagram illustrating the identification of studies through database and registry searches



3.2 Classification of porous systems for colon cancer therapy

This section categorizes porous systems intended for colon cancer therapy according to the International Union of Pure and Applied Chemistry (IUPAC) definition of porosity, which classifies materials based on their average pore diameter as follows:[9]
Microporous systems: pores with dimensions less than 2 nanometers (nm).
Mesoporous systems: pores having sizes between 2 and 50 nanometers.
Macroporous systems: pores with sizes exceeding 50 nm.
This IUPAC-based classification provides a structured framework for analyzing the relationship between pore size, drug permeability, and therapeutic efficacy in advanced drug delivery systems. It facilitates a detailed comprehension of how structural porosity influences diffusion behavior, drug release kinetics, and overall biological efficacy. Figure 2 demonstrates that the predominant materials are mesoporous, succeeded by macroporous and microporous types. Subsequent sections will elaborate on each porosity category, emphasizing their structural characteristics, drug release mechanisms, and biological implications pertinent to colon cancer therapy.[9]

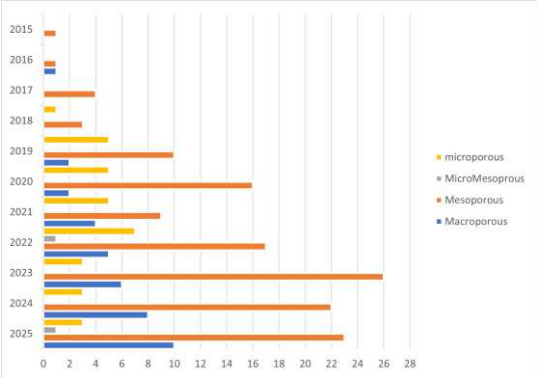
Figure 2The majority of materials fall within the mesoporous regime (132 samples, 65%), followed by macroporous structures (38 samples, 18%) and microporous structures (32 samples, 16%).



3.3. Analysis of yearly trends and their impact on data structure

The annual distribution of porous materials indicated that, recently, research efforts have predominantly focused on mesoporous systems. The excessive focus resulted in a markedly increased variance and noise level within the mesoporous subgroup, as these studies include a wide range of material types, drug categories, loading methods, and assay conditions. As a result, the raw IC_{50} dataset displayed significant heterogeneity, rendering direct cross-group comparisons invalid and statistically skewed.

Figure 3.Yearly distribution of porous



3.4 Variability of IC_{50} across pore categories

The analysis of IC_{50} values revealed significant variation within the groups of macroporous, mesoporous, and microporous designs. Macroporous materials exhibited a moderately broad range (range = 430 µM; median ≈ 24 µM; CV ≈ 1.66). Mesoporous systems had the greatest variability (range: 0.005–9354 µM; CV > 6), despite possessing the lowest median (~12 µM), influenced by severe outliers. Microporous structures demonstrated the most restricted range (~300 µM; CV = 1.50) while maintaining significant dispersion. The overlapping interquartile ranges across the three groups suggested an absence of a consistent or predicted correlation between pore size and cytotoxic efficacy.

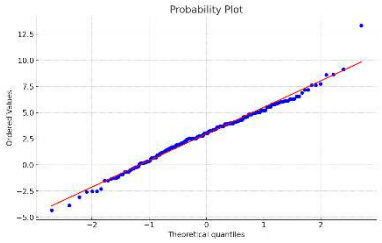
Table 1summarizes the range, median, IQR, SD, CV, and IQR-to-median values for macroporous, mesoporous, and microporous materials.

	Macroporous	Mesoporous	Microporous
Range	430.17	9353.99	428.50
Medien	24.53	12.25	33.95
IQR	43.36	44.43	68.89
SD	87.34	826.91	165.75
CV	1.66	6.52	1.69
IQR-Medien	1.76	3.62	2.03

3.4.1. Influence of publication trends and Data normalization

Recent work has indicated an overfocus on mesoporous formulations, resulting in increased variability within this subgroup due to differing chemistries, loading techniques, and test conditions. The Box–Cox transformation enhanced normality and diminished skewness; nonetheless, the heterogeneity resulting from methodological diversity remained and obstructed significant effect-size aggregation.

Figure 4QQ-plot showing improved IC_{50} normality after Box–Cox transformation, while persistent methodological heterogeneity across studies prevents meaningful effect-size pooling.



3.4.2. Meta analysis feasibility

The significant diversity in experimental design, drug classes, nanoplatforms, and particularly the disproportionate sample sizes across pore categories precluded the fulfillment of assumptions necessary for meta-analysis. Thus, the research employed ANOVA-based modeling augmented by structural machine-learning methodologies.

3.5. Two-Way ANOVA

The two-way ANOVA indicated a significant main effect of cell type on IC50_BoxCox values ($F = 5.96$, $p = 0.000689$). This signifies that drug sensitivity exhibits considerable variation among distinct cell lines, underscoring cell type as a crucial factor influencing IC50 variability. In accordance with this, significant disparities were noted in the mean IC50_BoxCox values: circulating tumor cells (CTCs) and RKO displayed the lowest values (−0.22 and −0.01, respectively), while SW480, Caco-2, and HT29 demonstrated markedly larger IC50 values, signifying reduced sensitivity.

The primary effect of pore type was not statistically significant ($F \approx 7.7\times10^{-13}$, $p = 1.0$). Despite the observation of tiny numerical differences, mesoporous materials exhibited marginally lower average IC50 values than microporous and macroporous structures; nonetheless, these variations lacked statistical significance. Consequently, pore architecture alone did not significantly influence overall IC50 variations.

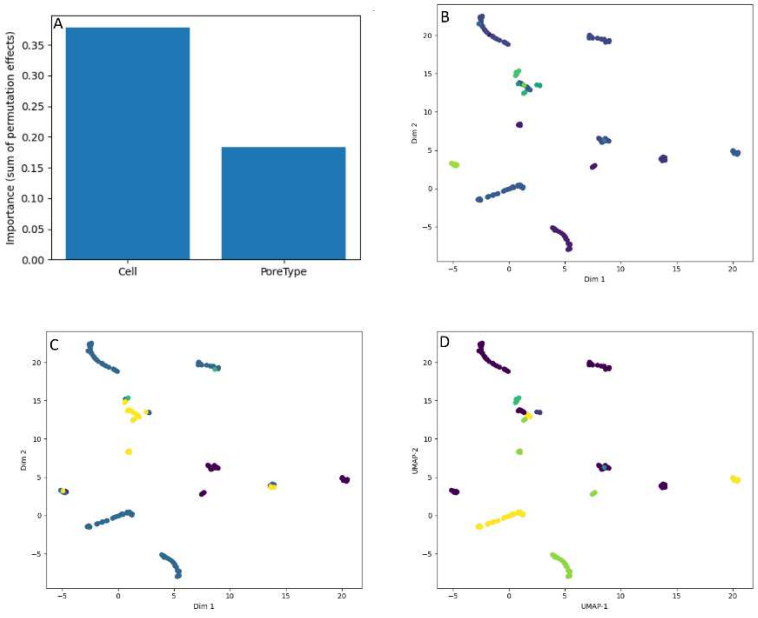
Although pore type did not show a significant main effect, the analysis of the interaction between cell type and pore type revealed distinct cell-specific patterns, indicating that the optimal pore type differed across cell lines.
Macroporous structures yielded the lowest IC50_BoxCox values for many cell lines (CT26, Caco-2, MC38, SW480, LS174T), whereas microporous materials proved most effective for others (HT29, RKO, SW489, LoVo, CTCs). Some cell lines, like SW620 and HeLa, responded best to mesoporous structures, while HCT116 had the lowest IC50 with mesoporous materials. These findings highlight a cell-dependent interaction, suggesting that the optimal pore type is not universal but changes with the cellular context.
Cell type showed a strong and statistically significant influence on the IC_{50}_BoxCox values.
In contrast, pore type did not exhibit a significant main effect.
These findings highlight the importance of considering the interaction between cell type and pore structure when evaluating material performance.

3.6. Machine learning based structural analysis

A thorough examination of linear, nonlinear, supervised, and unsupervised modeling frameworks—including predictive models (linear regression, random forest, XGBoost, SVR, Gaussian process, and MLP), feature importance methodologies, and nonlinear dimensionality-reduction techniques—revealed that the primary factor influencing drug-response variability (IC_{50}) is the biological identity of the cell line, rather than the pore type of the nanomaterial. All conventional and advanced predictive models had exceedingly inadequate performance, consistently yielding R^2 values close to zero. The multilayer perceptron accounted for merely 0.09–0.17 of the variance. The results suggest that the dataset contains a physiologically and physically intricate, low-signal structure that restricts overall prediction.
Despite the predictive models' general inability to replicate the variance structure, the permutation importance analysis in the MLP model yielded definitive insights into feature significance. The "Cell" variable had the greatest significance (0.38), whereas "Pore Type" displayed a notable yet lesser influence (0.18). This trend suggests that, even in nonlinear contexts, cell identity accounts for approximately twice the contribution of pore type to IC_{50} variability. Nonetheless, pore type is not insignificant; it serves as a minor yet discernible factor in the non-linear response landscape.
Unsupervised analysis yielded a very cohesive representation of the data's fundamental structure. UMAP demonstrated the most pronounced separation among all methodologies, elucidating distinctly defined and naturally occurring clusters that correspond to specific cell lines. Coloring the UMAP space by pore type revealed an absence of global patterns, independent clumping, and merely distributed low-intensity signals. t-SNE generated a nearly comparable structure, exhibiting distinct and persistent separation of cell lines without any clustering influenced by pore type. Kernel PCA (RBF kernel) produced a multi-cluster arrangement consistent with cell identification; however, there was no inherent categorization linked to pore type. The combined data indicate that pore type does not have significant structural influence on a wide scale and functions mainly as a contextual modulator within each cell line.
The self-organizing map (SOM) further substantiated the preeminence of cell-line architecture. Each cell line inhabited a unique area within the two-dimensional topological grid, affirming robust spatial organization at the biological level. Pore types were extensively distributed over the map and did not aggregate in any particular area. The lack of topological consistency for pore type signifies that it does not produce a distinct structural signature; rather, it acts as a secondary modifier integrated into the overarching cell-driven architecture of IC_{50} responses.
Gaussian Mixture Modeling (GMM) validated the patterns identified in prior structure-based techniques. The optimum model comprised seven components, signifying the existence of seven latent phenotypic states within the dataset. The latent components exhibited significant overlap with the cell-line clusters found via UMAP, and none aligned with a "pure pore-type cluster." This further substantiates that the underlying architecture of IC_{50} reactions is inherently cell-driven rather than pore-driven.
Although there are no global impacts, intracellular investigations revealed that pore type has a tangible, consistent, and reproducible impact inside each cell line. Mean IC_{50} values (Box–Cox

transformed) demonstrated distinctly cell-specific patterns: Macroporous nanomaterials exhibited superior performance in CT26, Caco-2, LS174T, MC38, and SW480, while microporous structures were most effective for HT29, RKO, SW489, LoVo (microporous), and CTCs. Mesoporous structures showed superiority in SW620, LoVo, Caco-2 (mesoporous), and HeLa-colon, but micro-mesoporous materials were distinctly best for HCT116. This observed variability signifies that pore-type effects are not universally weak; instead, they are markedly cell-specific and context-dependent. As a result, a universal ranking of pore types is absent among cell lines.
graphic 5 This four-panel graphic encapsulates machine-learning evidence—feature importance, UMAP embeddings, and GMM clustering. (A) The cell line exhibits greater significance than pore type in the MLP model. (B) Distinct UMAP clustering is influenced by cell identity. (C) There is no significant clustering based on pore type. (D) Gaussian Mixture Model components correspond to cell-line structure instead of pore type.

Figure 5 This four-panel figure summarizes machine-learning evidence—feature importance, UMAP embeddings, and GMM clustering **(A)** Greater importance of Cell Line compared to Pore Type in the MLP model.**(B)** Clear UMAP clustering driven *by cell identity.* ***(C)*** *No meaningful clustering by pore type.****(D)*** *GMM components aligning with cell-line structure rather than pore type.*



4.Discusosion

Cancer cannot be seen merely as a chemical phenomenon; instead, its behavior arises from the complexities of metabolic pathways and physical interactions. Every cancer cell line has distinct metabolic pathways, uptake mechanisms, and intracellular trafficking characteristics, while the chemical and structural attributes of porous carriers, such as composition, pore size, and surface interactions, dictate the interaction of these systems with the cellular environment. Therefore, a significant interpretation of treatment efficacy necessitates a comprehensive chemo-biological viewpoint.
A major problem with the current literature is that it is not consistent. While researchers have thoroughly investigated specific porous structures, particularly mesoporous systems, they still lack data for many cell lines. This disparity in material coverage and biological models limits the consistent generalizability of the results.
We expect that this study provides a unified chemo-biological framework and contributes to the development of more standardized and coherent research methodologies. This study aims to identify

certain porous materials and cell models that require further exploration, hence assisting future research in the systematic development of more efficient anticancer delivery methods.

5. Conclusion

The main conclusion is that pore type is not a key factor, but cell identity is the best predictor of IC_{50}. Our findings suggest that pore type has a merely secondary impact; thus, its actual function necessitates clarification through direct investigation of its effects on cellular mechanisms and drug-release dynamics.

AUTHORS CONTRIBUTIONS

Sana Tat participated in data collection and manuscript drafting, and contributed to the study design as well as the analysis and interpretation of results.

Ehsan Mohebbi was involved in data collection, data analysis, and interpretation of the results.

Dr. Alireza Akbarzadeh contributed to the study conception and design and assisted in drafting the manuscript.

All authors reviewed the findings, discussed the results, and approved the final version of the manuscript for publication

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CONFLICT OF INTERESTSTATEMENT
The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available on request from the corresponding author

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Supporting Information

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Table S1.

Year	Composite Name	IC_{50} (μg.mL⁻¹)	pore type	Category.	Ref.
2025	CMC/HAp/ Fe_3O_4	32	Macroporous	Unclear risk	[47]
2019	CS-DA/OP6 hydroge	0.24	Macroporous	Low risk	[48]
2025	Gd- CeO_2 NPs	200	Macroporous	High risk of bias	[49]
2024	GG–SFE–ε-PL hydrogel	3.5	Macroporous	Unclear risk	[50]
2022	FU-5/CV10	9.76	Macroporous	Low risk	[51]
2023	6MP-GPGel	36.01	Macroporous	Low risk	[52]
2025	ABZ nanosuspension	1.18	Macroporous	Low risk	[53]
2021	B-MSN (FU-5@MSN@EGCG/Fe^{3+})	25	Macroporous	Unclear risk	[54]
2025	B(ZT)bi-metal oxides ZnO–TiO_2	12.5	Macroporous	Unclear risk	[55]
2021	CAP-MSN)CHS-GCA	117.3	Macroporous	High risk of bias	[56]
2025	chitosan-based hydrogel	2.5	Macroporous	Unclear risk	[57]
2024	Cur@Lac GelMA/SilMA	50	Macroporous	Unclear risk	[58]
2024	f TQ-PB	80.59	Macroporous	Low risk	[59]
2016	ME/5FU	0.08	Macroporous	Low risk	[60]
2025	GN@CsNPs	30.9	Macroporous	Unclear risk	[61]
2025	GPCD hydrogels	10	Macroporous	Unclear risk	[62]
2024	FU-5-MHM	100	Macroporous	Unclear risk	[63]
2019	INUAAD10 gel	50	Macroporous	Unclear risk	[64]
2025	MHBs	64	Macroporous	Unclear risk	[65]
2022	MT/SD-hydrogel	24.075	Macroporous	Unclear risk	[66]
2024	MTX-MFM(Mannose-Fe_3O_4/MIL-88(Fe) (MFM))	300	Macroporous	High risk of bias	[46]
2021	PNiPenPH	35.6	Macroporous	Unclear risk	[67]
2020	Poloxamer 407 (Pluronic F127)	0.5	Macroporous	Unclear risk	[68]
2025	Poly(NIPAM-co-HEMA-co-AAm) hydrogel	6.15	Macroporous	Low risk	[69]
2022	Psy-g-Poly(An-co-AA)	40	Macroporous	Unclear risk	[70]
2024	PTX(8)@BN@Gel	1.48	Macroporous	Low risk	[71]
2024	PVA–κ-Carrageenan hydrogel modified with tannic acid	125	Macroporous	High risk of bias	[72]
2021	SP-SLS-NS	20.1	Macroporous	Unclear risk	[73]

2023	Te/V-HAP@DOX-CS	0.26	Macroporous	Low risk	[74]
2023	ZnF	25	Macroporous	Unclear risk	[75]
2023	ACNF-VD-containing composite aerogel	141.2	Mesoporous	High risk of bias	[76]
2024	BA-rMSNs	0.26	Mesoporous	Low risk	[77]
2025	$CaCO_3$/CNF/SA hydrogels	16	Mesoporous	Unclear risk	[78]
2022	CS-ID@NMs + US	0.2	Mesoporous	Unclear risk	[79]
2015	NPCPT	54.75	Mesoporous	Low risk	[80]
2025	Cu/EA-MOF	60	Mesoporous	Unclear risk	[81]
2019	Cur-MSNPs	4	Mesoporous	Unclear risk	[82]
2021	DOX- Fe_3O_4@agar.	12	Mesoporous	Unclear risk	[83]
2023	doxorubicin-loaded hydrogel (50 -GMP: NAP, 16.0 mM: 4.0 mM, DOX 0.2 mM	2	Mesoporous	Unclear risk	[84]
2023	Eud-Coated TER-Loaded MSNs(SBA-15)	4.38	Mesoporous	Low risk	[85]
2021	MCFL224 nano-complexes(MOF)	1.9	Mesoporous	Unclear risk	[86]
2023	MCM*NH2 *HN*Cu (Cu (II)-hybrid)	70	Mesoporous	Unclear risk	[87]
2019	Oxmi-HMSN	5.68	Mesoporous	Low risk	[88]
2020	S-MTN@IG-P	30	Mesoporous	Unclear risk	[89]
2025	DOX@MSNP-BA-Tf	140	Mesoporous	High risk of bias	[2]
2025	(OXP/CDs/PS)@Pec hydrogel beads	50	Mesoporous	Unclear risk	[90]
2023	(Zn-MSN-NH_2-CP)	250	Mesoporous	High risk of bias	[91]
2021	5-FC loaded G. Mg/Clino	150	Mesoporous	High risk of bias	[92]
2025	5-Flu/MET@MSNs/Ce6@HIL	1.29	Mesoporous	Low risk	[93]
2020	FU-5 + CUR@CS/Gr/Pd	9.87	Mesoporous	Low risk	[94]
2022	FU-5 loaded Mg/Ca(NRs)	165	Mesoporous	High risk of bias	[95]
2021	FU-5-MS5)CHS-GCA	26.15	Mesoporous	Low risk	[96]
2017	FU-5@MSN-RGD	25.86	Mesoporous	Low risk	[97]
2018	FU-5@MSN–NH_2/GC	1.25	Mesoporous	Low risk	[98]
2022	FU-5/Cur-P@HMPB	10	Mesoporous	Unclear risk	[99]
2025	A-OHEC-APTES@1	25	Mesoporous	Unclear risk	[100]
2025	A(ZT) bi-metal oxides ZnO–TiO_2	12	Mesoporous	Unclear risk	[55]
2021	AFt–Cu	4.92	Mesoporous	Low risk	[101]
2024	Ag/MSS/Cpt	15	Mesoporous	Unclear risk	[102]
2023	Apt-PEG-Au-NPs@FU-5	11.27	Mesoporous	Low risk	[103]

2020	Apt–PCAD–DMSN@DOX	6.25	Mesoporous	Low risk	[104]
2021	AuNPs–LY@Ge	0.056	Mesoporous	Unclear risk	[105]
2020	BGN@PDA-DOX	30	Mesoporous	Unclear risk	[106]
2019	BisBAL NPs t	5	Mesoporous	Unclear risk	[107]
2025	CH/HA PECs	18.15	Mesoporous	Low risk	[108]
2023	CaO_2–N770@MSN	3	Mesoporous	Unclear risk	[109]
2023	Carboplatin@N-HMSNs	30.47	Mesoporous	Low risk	[110]
2022	CatCry-AgNP-DOX	0.8	Mesoporous	Unclear risk	[111]
2019	CeO_2 NPs	31.925	Mesoporous	Unclear risk	[112]
2020	CFAP = COF + $FeCl_3$ + Poly(*p*-phenylenediamine) + PEG (NH_2-PEG_{2000}-COOH)	100	Mesoporous	Unclear risk	[113]
2023	Cisplatin@N-HMSNs	20.75	Mesoporous	Low risk	[110]
2023	CMC@MWCNTs@FCA	752	Mesoporous	High risk of bias	[114]
2019	CMC/LDH(Zn/Al)-FU-5	32	Mesoporous	Unclear risk	[115]
2023	CMS-Glu/SHK	0.666	Mesoporous	Unclear risk	[116]
2022	CMS@LDH(Mg–Al)@DOX,FU-5 microspheres	36	Mesoporous	Unclear risk	[117]
2020	CNT–DOX–Fe_3O_4–Tf	0.377	Mesoporous	Unclear risk	[118]
2023	CoF	30	Mesoporous	Unclear risk	[75]
2023	COF/FU-5@CMS-Gel hydrogel	70	Mesoporous	Unclear risk	[119]
2023	Col-IV@IRI-G5MNP	23.9	Mesoporous	Unclear risk	[120]
2020	$Gd_{1-x-\gamma}Ce_xTb_\gamma BO_3$@$SiO_2$	10	Mesoporous	Unclear risk	[121]
2025	CP@MSN/PB + NIR	5	Mesoporous	Unclear risk	[122]
2023	CsDAGG13/ Asp/Cur hydrogels	32	Mesoporous	Unclear risk	[123]
2025	Cu–GA/DOX@ZIF-8 (CGDZ)	2	Mesoporous	Unclear risk	[124]
2023	CuF	15	Mesoporous	Unclear risk	[75]
2020	CuS@Fe-MOF	0.4	Mesoporous	Unclear risk	[125]
2025	DMSN@Pla-Lipo	3.7	Mesoporous	Unclear risk	[126]
2023	DOX-Gel.	2	Mesoporous	Unclear risk	[84]
2021	Dox@IO-MMNs	6.93	Mesoporous	Low risk	[127]
2025	DSMC@PDA-HA	60	Mesoporous	Unclear risk	[128]
2023	Dy-NiCuZn NSFs (0.02)	144.92	Mesoporous	High risk of bias	[129]
2017	EC-MSN-D	7	Mesoporous	Unclear risk	[130]
2023	erogel–Cur–PLP	80	Mesoporous	Unclear risk	[131]

2024	Fe_3O_4-NPs	60	Mesoporous	Unclear risk	[132]
2024	GelMA-BOSU-NG	0.6	Mesoporous	Unclear risk	[133]
2024	Fe_3O_4@PDA@$CaCO_3$@CM	150	Mesoporous	High risk of bias	[134]
2021	Fe_3O_4/MSN–NH_2	3.2	Mesoporous	Unclear risk	[135]
2024	CMD-BOSU-NG	0.5	Mesoporous	Unclear risk	[133]
2023	Fu-5 loaded b-CD/Di	200	Mesoporous	High risk of bias	[136]
2023	FU.FA@NS	0.5	Mesoporous	Unclear risk	[137]
2022	FU#(PICCS@Pd)#DOX	0.85	Mesoporous	Low risk	[138]
2022	FX@Fe_3O_4–mSiO_2–TA	80	Mesoporous	Unclear risk	[139]
2025	Gd0.825Eu0.175B3O6@HAP@PEG	12.5	Mesoporous	Unclear risk	[140]
2022	GDH-N/C	0.7	Mesoporous	Unclear risk	[141]
2021	DOX@GeMSNs	1.77	Mesoporous	Low risk	[142]
2024	Gi-Ag@NMOF–CS–FA	0.01	Mesoporous	Low risk	[143]
2021	DOX@GMTMSNs	1.891	Mesoporous	Unclear risk	[144]
2019	GOPEG-PCACA-FA	50.69	Mesoporous	Low risk	[145]
2024	HA-BOSU-NG	0.3	Mesoporous	Unclear risk	[133]
2025	HA@HMn/PMS	120	Mesoporous	High risk of bias	[146]
2018	HA/FMSN	1.08	Mesoporous	Low risk	[147]
2020	HAP-P-Pip9.3-GA-FA	2.4	Mesoporous	Unclear risk	[148]
2024	HAp/PANI/TD/DOX.	1.42	Mesoporous	Low risk	[149]
2024	HCPT@ZIF-90-PEG-FA	3	Mesoporous	Unclear risk	[150]
2017	HMSN	1.19	Mesoporous	Low risk	[151]
2020	HMSN-11	50	Mesoporous	Unclear risk	[6]
2020	HMSS–N=N–CS/DOX + Colon enzymes	9.41	Mesoporous	Low risk	[152]
2019	hollow CeO_2	24.075	Mesoporous	Unclear risk	[112]
2019	hollow CeO_2/SiO	18.625	Mesoporous	Unclear risk	[112]
2024	Hollow Mesoporous Calcium Peroxide (HMCPN17)	400	Mesoporous	High risk of bias	[153]
2020	HPAE-PCL- b -MPEG	1000	Mesoporous	High risk of bias	[154]
2023	HSCuPPaCC	38.9	Mesoporous	Unclear risk	[155]
2025	ICT-BTO@MSNs@HA	6.25	Mesoporous	Low risk	[156]
2020	M(abc)-DOX@PDA-ICG-PEG-RGD	4	Mesoporous	Unclear risk	[157]
2025	MA@E liposomes	0.03	Mesoporous	Low risk	[158]
2018	MCM-41–PO_3–VOR	6.3	Mesoporous	Unclear risk	[159]

2016	MCM-48	400	Mesoporous	High risk of bias	[160]
2024	MET&3-BrPA@ZIF-90@F127 (M&B@MOF)	20.2	Mesoporous	Unclear risk	[161]
2022	MMSN-EDTA@HA-Pt	8.03	Mesoporous	Low risk	[162]
2025	MNPs/DOX	10	Mesoporous	Unclear risk	[163]
2023	MPDA-Fe(III)-DOX-HA-NIR	15	Mesoporous	Unclear risk	[164]
2022	MS@FU-5#Azo	4.6	Mesoporous	Unclear risk	[165]
2025	MSN-S–S-ALG@Cur/Q	76.62	Mesoporous	Low risk	[166]
2017	MSNPs-Rh_2-FITC	7.5	Mesoporous	Unclear risk	[167]
2022	MSNs-DOX	15	Mesoporous	Unclear risk	[168]
2024	MSNs-PDPA-co-PGMA	733	Mesoporous	High risk of bias	[169]
2024	MSNs@NH_2-CLB	27.67	Mesoporous	Low risk	[170]
2020	MSNsPCOL/CG-FA	17.4	Mesoporous	Unclear risk	[171]
2024	NH2-MIL-101(Fe)@GO@Luteolin@Matrine (MGD)	70	Mesoporous	Unclear risk	[172]
2025	NiO-CMC-Dcar	10	Mesoporous	Unclear risk	[173]
2022	NMOF-CS-FA-MTX	0.005	Mesoporous	Unclear risk	[174]
2023	OX@Se-MnP	65	Mesoporous	Unclear risk	[175]
2023	Oxalipalladium@N-HMSNs	42.82	Mesoporous	Low risk	[110]
2023	Oxaliplatin@N-HMSNs	19.28	Mesoporous	Low risk	[110]
2019	P3DL/PAH/PSSCMA	25	Mesoporous	Unclear risk	[176]
2022	PBNC60@m-SiO_2@HA@DOX	21	Mesoporous	Unclear risk	[177]
2024	PCDP (HPB@CaO₂/DOX-PAA)	10	Mesoporous	Unclear risk	[178]
2025	pure hydrogel(AmPec-GAA15)	2.5	Mesoporous	Unclear risk	[179]
2022	Fe-BDC-PEG@FU-5	18	Mesoporous	Unclear risk	[180]
2024	RA	65	Mesoporous	Unclear risk	[181]
2025	SA/HAp-Fe_3O_4	32	Mesoporous	Unclear risk	[182]
2019	SPASNs@DOX@AS1411	5	Mesoporous	Unclear risk	[183]
2024	SPION@MSN-EPI/pDNA-ZIF-8-PEG-Apt	12	Mesoporous	Unclear risk	[184]
2022	St@Fu-5@GQDs@Bio-MOF	6.15	Mesoporous	Low risk	[185]
2025	Sul-IRMOF-ACA-HA@Sily	9.35	Mesoporous	Low risk	[186]
2025	Syloid 244FP #F3	40	Mesoporous	Unclear risk	[187]
2024	TPZ@Cu_2Cl$(OH)_3$-HA (TCuH)	100	Mesoporous	Unclear risk	[188]
2024	ZnO-chitosan nanocomposite	9354	Mesoporous	High risk of bias	[189]

2025	FU-5@SiO_2	37.78	microporous	Low risk	[190]
2019	DOX-loaded MANP-N 3 -FA	120	microporous	High risk of bias	[191]
2020	HKUST-1	12.5	microporous	Unclear risk	[192]
2021	PEG-Au-NPs@DOX	9.72	microporous	Low risk	[193]
2021	FU-5-loaded CMC/PAA/St-Fe3O4 3%	32	microporous	Unclear risk	[194]
2021	FU-5@LTL	0.06	microporous	Low risk	[195]
2022	FU-5@MOF-801	65.55	microporous	Low risk	[196]
2018	FU-5@MSN–NH2/GC+LV@MSN–COOH/GC on	7	microporous	Unclear risk	[197]
2021	FU-5@NaY	0.06	microporous	Low risk	[195]
2019	FU-5-AMSN-Alg/FA-CMCT-Gel-BDC	20	microporous	Unclear risk	[198]
2025	Apt-PEG-MOF@DOX	1.4	microporous	Unclear risk	[199]
2020	COF-B + Laser	60	microporous	Unclear risk	[200]
2020	COF@ICG@OVA(CIO + PDT)	12.5	microporous	Unclear risk	[201]
2023	CS/OD/MTX/TFPM	14	microporous	Unclear risk	[201]
2025	Dox/PAA-ZIF-8-3	2.85	microporous	Low risk	[202]
2024	GG@CsNP3/FU-5 hydrogel	6	microporous	Unclear risk	[203]
2020	magMOF@GOD	0.8	microporous	Unclear risk	[204]
2022	Magnetic UiO-66-NH_2 (MU)(OX)	18.47	microporous	Low risk	[205]
2024	MIL-125-NH_2	1.2	microporous	Unclear risk	[206]
2022	MSN-NH_2-Cur-AOS	30	microporous	Unclear risk	[207]
2022	OXA-CuS@UiO-66-NH_2	7.97	microporous	Low risk	[208]
2024	PCN-224/Au-NPs	300	microporous	High risk of bias	[209]
2022	Pectin/curcumin@bio-MOF-11	10	microporous	Unclear risk	[210]
2023	PEI-Se-MCM41@FU-5 (PBS)	24.6	microporous	Unclear risk	[211]
2023	Res@ZIF-8/TA	5	microporous	Unclear risk	[212]
2019	Faujasite-NaX (ZX)	168.3	microporous	High risk of bias	[213]
2022	TANEB hydrogel	16.38	microporous	Low risk	[214]
2022	TMU-6(RL1)	100	microporous	Unclear risk	[215]
2019	Zeolite A (ZA)	127.6	microporous	High risk of bias	[213]
2021	ZIF-8 NPs	35	microporous	Unclear risk	[216]
2020	$Zr_6O_4(OH)_4(TCPP)_3$ (PCN-223 MOF)	70	microporous	Unclear risk	[217]
2019	ZSM-5	170.8	microporous	High risk of bias	[213]

2022	TrzTFPPOP	3.25	MicroMesoporous	Low risk	[218]
2025	COF@IRI	40	MicroMesoporous	Unclear risk	[219]

References

[1] S. L. Tao and T. A. Desai, *Advanced drug delivery reviews* **2003**, *55*, 315–328.
[2] H. Y. Lee, N. Thirumalaivasan and S. P. Wu, *ACS Applied Bio Materials* **2025**.
[3] Q. An, Z. Dai, J. Zhang, H. Hu and J. Wang, *ACS Applied Nano …* **2024**.
[4] J. Gao, M. Li, H. Chen, Z. Xu, J. Li and Y. Kong, *Journal of Industrial and …* **2025**.
[5] F. Al-Sahlawi, I. Al-Ani, M. El-Tanani and H. A. Farooq, *Pharmacia* **2024**.
[6] M. Pérez-Garnes, M. Gutiérrez-Salmerón, V. Morales, A. Chocarro-Calvo, R. Sanz, C. García-Jiménez and R. A. García-Muñoz, *MATERIALS SCIENCE AND ENGINEERING C-MATERIALS FOR BIOLOGICAL APPLICATIONS* **2020**, *112*.
[7] V. Cauda, L. Mühlstein, B. Onida and T. Bein, *Microporous and Mesoporous Materials* **2009**, *118*, 435–442.
[8] M. Arruebo, *Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology* **2012**, *4*, 16–30.
[9] T. Mays in *A new classification of pore sizes*, *Vol. 160* Elsevier, **2007**, pp. 57–62.
[10] L. Yang, J. S. Chu and J. A. Fix, *International journal of pharmaceutics* **2002**, *235*, 1–15.
[11] P. Tugwell and D. Tovey in *PRISMA 2020*, *Vol. 134* Elsevier, **2021**, pp. A5–A6.
[12] H. Kuhn, S. Braslavsky and R. Schmidt, *Pure Appl. Chem* **2004**, *76*, 2105–2146.
[13] C. Beeri, P. A. Bernstein and N. Goodman in *A sophisticate's introduction to database normalization theory*, Elsevier, **1989**, pp. 468–479.
[14] G. W. Caldwell, Z. Yan, W. Lang and J. A. Masucci, *Current topics in medicinal chemistry* **2012**, *12*, 1282–1290.
[15] J. Osborne, *Practical Assessment, Research, and Evaluation* **2010**, *15*.
[16] J. I. Marden, *Statistical Science* **2004**, 606–614.
[17] S. J. Richter and M. E. Payton, *Journal of Applied Statistical Science* **2005**, *14*, 225–235.
[18] S. Kuntz, U. Wenzel and H. Daniel, *European journal of nutrition* **1999**, *38*, 133–142.
[19] B. K. Slinker, *Journal of molecular and cellular cardiology* **1998**, *30*, 723–731.
[20] R. Dunpall and N. Revaprasadu, *Toxicology Research* **2016**, *5*, 1078–1089.
[21] in *Pore-size–dependent performance of porous drug-delivery platforms in colorectal cancer: A PRISMA-aligned systematic review*, *Vol.* **2025**.
[22] H.-J. Vogel and K. Roth, *Advances in water resources* **2001**, *24*, 233–242.
[23] A. Rohatgi in *WebPlotDigitizer*, *Vol.* Austin, Texas, USA, **2017**.
[24] V. H. Sheth, N. P. Shah, R. Jain, N. Bhanushali and V. Bhatnagar, *The Journal of Prosthetic Dentistry* **2024**, *131*, 1038–1042.
[25] N. Roth, J. Zilliacus and A. Beronius, *Frontiers in Toxicology* **2021**, *3*, 746430.
[26] R. Gibert, M. Alberti, B. Poirier, C. Jallet, N. Tordo and S. Morgeaux, *Vaccine* **2013**, *31*, 6022–6029.
[27] X. Wan, W. Wang, J. Liu and T. Tong, *BMC medical research methodology* **2014**, *14*, 135.
[28] O.-w. ANOVA, *Group* **2008**, *1*, 3.
[29] J. G. Carbonell, R. S. Michalski and T. M. Mitchell, *Machine learning* **1983**, 3–23.
[30] J. Groß, *Linear regression*, Springer Science & Business Media, **2003**, p.

[31] L. Breiman, *Machine learning* **2001**, *45*, 5–32.
[32] T. Chen, T. He, M. Benesty, V. Khotilovich, Y. Tang, H. Cho, K. Chen, R. Mitchell, I. Cano and T. Zhou, *R package version 0.4-2* **2015**, *1*, 1–4.
[33] Z. Xu, Y. Gao and Y. Jin, *International Journal of Multimedia and Ubiquitous Engineering* **2014**, *9*, 67–80.
[34] D. J. MacKay, *NATO ASI series F computer and systems sciences* **1998**, *168*, 133–166.
[35] H. Taud and J.-F. Mas in *Multilayer perceptron (MLP)*, Springer, **2017**, pp. 451–455.
[36] L. McInnes, J. Healy and J. Melville, *arXiv preprint arXiv:1802.03426* **2018**.
[37] W. Song, L. Wang, P. Liu and K.-K. R. Choo, *Multimedia Tools and Applications* **2019**, *78*, 4311–4326.
[38] S. Mika, B. Schölkopf, A. Smola, K.-R. Müller, M. Scholz and G. Rätsch, *Advances in neural information processing systems* **1998**, *11*.
[39] D. Berkowitz, J. S. Cohen, N. McCollum, C. R. Rojas and J. M. Chamberlain, *The American journal of emergency medicine* **2023**, *74*, 130–134.
[40] P. S. Abhari and B. Habibi, *Crystal Growth &Design* **2024**.
[41] S. Song, D. Wang, K. Zhao, Y. Wu, P. Zhang and J. Liu, *Chemical Engineering …* **2022**.
[42] P. Mehta[1], K. Mahadik and S. Kadam, *Applications of Advanced …* **2020**.
[43] P. Jiang, Y. Hu and G. Li, *Talanta* **2019**, *200*, 212–217.
[44] E. Martínez, M. Osorio, C. Finkielstein and I. Ortíz, *International Journal of …* **2022**.
[45] S. Huang and G. Huang, *Journal of Drug Delivery Science and Technology* **2020**.
[46] H. Poursadegh, M. S. Amini-Fazl and S. Javanbakht, *International Journal of …* **2024**.
[47] R. Foroutan, A. Mohammadzadeh and R. Mohammadi, *Chemical Papers* **2025**.
[48] Y. Liang, X. Zhao, P. X. Ma, B. Guo, Y. Du and X. Han, *Journal of Colloid and Interface Science* **2019**, *536*, 224–234.
[49] S. Sarangi, U. Suryakanta, N. Nayak and D. Mandal, *Journal of Rare …* **2025**.
[50] Y. Qu, X. Li, X. Chen, J. Li, Z. Yu and R. Shen, *Journal of the Science of Food and Agriculture* **2024**, *104*, 9423–9433.
[51] N. Salahuddin, S. Awad and M. Elfiky, *RSC advances* **2022**.
[52] S. Kim, W. Lee, H. Park and K. Kim, *Gels* **2023**.
[53] Y. Guo, H. J. Patel, A. S. Patel, E. Squillante and K. Patel, *Colloids and Surfaces B: Biointerfaces* **2025**, *245*.
[54] Z. X. Chen, J. L. Li, P. Pan, P. Bao, X. Zeng and X. Z. Zhang, *NANO TODAY* **2021**, *41*.
[55] M. M. Khalaf, S. Shaaban and H. M. A. El-Lateef, *New Journal of …* **2025**.
[56] R. Narayan, S. Gadag, S. P. Cheruku and A. M. Raichur, *Carbohydrate …* **2021**.
[57] L. Wang, Z. Mei, G. Jin, H. Liu, S. Lv, R. Fu, M. Li and C. Yao, *Bioactive Materials* **2024**, *36*, 541–550.
[58] B. Zhang, J. Yan, Y. Jin, Y. Yang and X. Zhao, *European Journal of Pharmaceutics and Biopharmaceutics* **2024**, *202*.
[59] M. Alfatama, H. Choukaife, O. A. Rahal and N. Z. M. Zin, *Pharmaceutics* **2024**.
[60] H. Sadeghi-Abandansari, S. Pakian, M. R. Nabid, M. Ebrahimi and A. Rezalotfi, *European Polymer Journal* **2021**, *157*.
[61] M. A. Abdelaziz, A. I. Alalawy, M. Sobhi and O. M. Alatawi, *International Journal of …* **2025**.
[62] X. Q. Jia, Y. F. Wei, X. Y. Zhang, Q. P. Gu, Y. S. Liu, S. G. Wang and C. P. Zhu, *CHEMISTRY-AN ASIAN JOURNAL* **2025**.
[63] H. Poursadegh, V. Bakhshi, M. S. Amini-Fazl, Z. Adibag, F. Kazeminava and S. Javanbakht, *INTERNATIONAL JOURNAL OF BIOLOGICAL MACROMOLECULES* **2024**, *274*.
[64] F. Afinjuomo, P. Fouladian, A. Parikh, T. G. Barclay, Y. Song and S. Garg, *Pharmaceutics* **2019**, *11*.
[65] S. Tahmasebi and H. Farmanbordar, *International Journal of …* **2025**.

[66] C. Y. Wang, M. Sun, Z. Fan and J. Z. Du, *Chinese Journal of Polymer Science* **2022**.
[67] G. Carreño, A. Pereira, F. Avila-Salas, A. Marican, F. Andrade, M. M. Roca-Melendres, O. Valdés, S. Vijayakumar, S. Schwartz, I. Abasolo, D. Rafael and E. F. Durán-Lara, *MATERIALS SCIENCE & ENGINEERING C-MATERIALS FOR BIOLOGICAL APPLICATIONS* **2021**, *131*.
[68] C. K. Chung, J. García-Couce, Y. Campos, D. Kralisch, K. Bierau, A. Chan, F. Ossendorp and L. J. Cruz, *Molecules* **2020**, *25*, 2219.
[69] S. Ghasemi, M. Najafi, M. Doroudian, B. Rastegari, A. Behzad-Behbahani, H. Soltanimehr and F. Farjadian, *Gels* **2025**, *11*, 227.
[70] D. Kumar, A. Gautam and P. P. Kundu, *Journal of Applied Polymer …* **2022**.
[71] T. Wang, J. Ding, Z. Chen, Z. Zhang and Y. Rong, *… applied materials & …* **2024**.
[72] A. Marlina, M. Misran, S. Ndruru and H. M. Saad, *…* **2024**.
[73] S. Taymouri, Z. Ahmadi and M. Mirian, *Pharmaceutical …* **2021**.
[74] M. A. Hady and M. K. Ahmed, *Egyptian Journal of Chemistry* **2023**.
[75] S. Mohana and S. Sumathi, *Journal of Cluster Science* **2024**.
[76] O. Bingol Ozakpinar, H. Dastan, M. Gurboga, F. S. Sayin, D. Ozsavci and E. Caliskan Salihi, *Gels* **2023**, *9*.
[77] Y. Fan, W. Zhang, Z. Iqbal, X. Li, Z. Lin, Z. Wu and Q. Li, *Lipids in Health and …* **2024**.
[78] W. Bai, H. Chen, J. Li, W. Cai, Y. Kong and X. Zuo, *International Journal of Biological Macromolecules* **2025**, *309*, 142839.
[79] Y. Cao, S. Liu, Y. Ma, L. Ma, M. Zu, J. Sun, F. Dai and L. Duan, *Small* **2022**.
[80] C. Théron, A. Gallud, S. Giret, M. Maynadier, D. Grégoire, P. Puche, E. Jacquet, G. Pop, O. Sgarbura and V. Bellet, *RSC Advances* **2015**, *5*, 64932–64936.
[81] W. Zhang, M. Zhao, L. Wang, J. Wang, X. Ge, J. Liu, B. Chen, S. Gao and J. Lu, *iScience* **2025**, *28*.
[82] N. S. Elbialy, E. A. Elfatah and W. A. Khalil, *EGYPTIAN JOURNAL OF CHEMISTRY* **2019**, *62*, 125–135.
[83] Y.-J. Wang, P.-Y. Lin, S.-L. Hsieh, R. Kirankumar, H.-Y. Lin, J.-H. Li, Y.-T. Chen, H.-M. Wu and S. Hsieh, *Materials* **2021**, *14*, 1824.
[84] Umesh, S. Sarkar, S. Bera, P. Moitra and S. Bhattacharya, *MATERIALS TODAY CHEMISTRY* **2023**, *30*.
[85] M. H. Alyami, A. A. Musallam, T. M. Ibrahim, M. A. Mahdy, H. M. Elnahas and R. A. Aldeeb, *Pharmaceutics* **2023**, *15*.
[86] N. Mokri, Z. Sepehri, F. Faninam, S. Khaleghi, N. M. Kazemi and M. Hashemi, *Gene Therapy* **2022**, *29*, 680–690.
[87] A. Naz, R. Kumari, S. Arun, S. S. Narvi and M. S. Alam, *Journal of Polymer …* **2023**.
[88] H. Yang, Y. Liu, Y. Qiu, M. Ding and Y. Zhang, *International Journal of Pharmaceutics* **2019**, *566*, 585–593.
[89] M. Gautam, B. Gupta, Z. C. Soe and K. Poudel, *Pharmaceutical …* **2020**.
[90] M. Pooresmaeil and H. Namazi, *Industrial Crops and Products* **2025**, *223*, 120124.
[91] H. Sinafar, H. Noorbazargan and F. Tafvizi, *Journal of Nanoparticle …* **2023**.
[92] S. I. Othman, A. A. Allam and H. A. Fassam, *Journal of Inorganic and …* **2021**.
[93] N. Wang, J. Hu, L. Jin, S. Wang, B. Zeng, Y. Liu, A. Jin, J. Piao, L. Chen and W. Huang, *International Journal of Biological Macromolecules* **2025**, *304*, 140996.
[94] S. Dhanavel, P. Praveena, V. Narayanan and A. Stephen, *Polymer Bulletin* **2020**.
[95] S. I. Othman, A. Adlii, A. A. Allam and H. A. Alqhtani, *Journal of Inorganic and …* **2022**.
[96] R. Narayan, S. Gadag, R. J. Mudakavi, S. Garg, A. M. Raichur, Y. Nayak, S. G. Kini, K. S. R. Pai and U. Y. Nayak, *Journal of Drug Delivery Science and Technology* **2021**, *63*, 102472.

[97] G. Pan, T. T. Jia, Q. X. Huang, Y. Y. Qiu, J. Xu, P. H. Yin and T. Liu, *Colloids and Surfaces B: Biointerfaces* **2017**, *159*, 375–385.
[98] W. Liu, Y. C. Zhu, F. Wang, X. Li, X. J. Liu, J. J. Pang and W. S. Pan, *ROYAL SOCIETY OPEN SCIENCE* **2018**, *5*.
[99] J. Chen, F. Xue, W. Du, H. Yu, Z. Yang, Q. Du and H. Chen, *Nano Letters* **2022**.
[100] Q. Cheng, H. Fu and Y. Mao, *Journal of Medical and Biological Engineering* **2025**.
[101] K. Xiong, Y. Zhou, J. Karges, K. Du and J. Shen, *... Applied Materials & ...* **2021**.
[102] S. Rehman, V. Ravinayagam, S. S. Al-Jameel, S. M. Ali, S. Z. Alzayer, Z. M. Alfaraj, A. Alboeid, N. Alamri, S. H. Al Isam and H. Dafallae, *Arabian Journal of Chemistry* **2024**, *17*, 105661.
[103] A. K. M. Al-Mosawi and A. R. Bahrami, *... in Bioengineering and ...* **2023**.
[104] M. Zahiri, M. Babaei, K. Abnous, S. M. Taghdisi, M. Ramezani and M. Alibolandi, *JOURNAL OF CELLULAR PHYSIOLOGY* **2020**, *235*, 1036–1050.
[105] S. Managò, C. Tramontano, D. D. Cave and G. Chianese, *Small* **2021**.
[106] Y. Xue, W. Niu, M. Wang, M. Chen, Y. Guo and B. Lei, *ACS Nano* **2020**, *14*, 442–453.
[107] C. Cabral-Romero, J. M. Solís-Soto, Y. Sánchez-Pérez, N. Pineda-Aguilar, I. Meester, E. Pérez-Carrillo, S. E. Nakagoshi-Cepeda, R. I. Sánchez-Nájera, M. A. Nakagoshi-Cepeda and R. Hernandez-Delgadillo, *Anti-cancer drugs* **2020**, *31*, 251–259.
[108] N. M. E. Elsayyad, M. S. Ibrahim and S. H. Noshi, *Journal of Drug Delivery Science ...* **2025**.
[109] J. Wu, S. Yi, Y. Cao, M. Zu, B. Li, W. Yang, M.-A. Shahbazi, Y. Wan, R. L. Reis and S. C. Kundu, *Biomaterials* **2023**, *302*, 122332.
[110] M. E. Moghadam, M. Sadeghi, H. Mansouri-Torshizi and M. Saidifar, *European Journal of Pharmaceutical Sciences* **2023**, *187*, 106477.
[111] R. Zhou, T. Y. Ohulchanskyy, Y. Xu and R. Ziniuk, *... Applied Materials & ...* **2022**.
[112] Z. Rasouli, M. Yousefi, M. B. Torbati, S. Samadi and K. Kalateh, *Polyhedron* **2020**, *176*, 114297.
[113] S. Liu, Y. Zhou, C. Hu, L. Cai and M. Pang, *ACS Applied Materials & ...* **2020**.
[114] M. H. Alizadeh, M. Pooresmaeil and H. Namazi, *International Journal of Biological Macromolecules* **2023**, *234*, 123778.
[115] M. Pooresmaeil, S. Behzadi Nia and H. Namazi, *International Journal of Biological Macromolecules* **2019**, *139*, 994–1001.
[116] X. Wang, W. Guo, J. Han, J. Li, Q. Zhao and Y. Mao, *Colloids and Surfaces B ...* **2023**.
[117] E. Ranjbar, H. Namazi and M. Pooresmaeil, *INTERNATIONAL JOURNAL OF BIOLOGICAL MACROMOLECULES* **2022**, *201*, 193–202.
[118] S. S. Andhari, R. D. Wavhale, K. D. Dhobale and B. V. Tawade, *Scientific reports* **2020**.
[119] M. Pooresmaeil and H. Namazi, *Industrial Crops and Products* **2023**, *202*, 117102.
[120] S. Chauhan, R. Solanki, A. K. Jangid, P. Jain, P. Pranjali, S. Patel, A. Guleria, D. Pooja and H. Kulhari, *Journal of Industrial and Engineering Chemistry* **2023**, *128*, 258–267.
[121] P. Akman, S. Ulusan, S. Banerjee and A. Yilmaz, *Microporous and Mesoporous ...* **2020**.
[122] Z. H. Wang, X. Zeng, W. Huang, Y. Yang and S. Zhang, *Nature ...* **2025**.
[123] G. Dalei, S. Das, S. R. Jena, D. Jena, J. Nayak and L. Samanta, *Chemical Engineering Science* **2023**, *269*, 118482.
[124] G. T. Q. Vu, L. M. Nguyen and K. N. N. Do, *ACS Applied Bio ...* **2025**.
[125] Z. Wang, W. Yu, N. Yu, X. Li, Y. Feng, P. Geng, M. Wen, M. Li, H. Zhang and Z. Chen, *Chemical Engineering Journal* **2020**, *400*, 125877.
[126] Y. Yuan, Q. Lin, H. Y. Feng, Y. Zhang and X. Lai, *Nature ...* **2025**.
[127] K. El-Boubbou, R. Ali, S. Al-Humaid, A. Alhallaj, O. Lemine, M. Boudjelal and A. AlKushi, *Pharmaceutics* **2021**, *13*, 553.

[128] G. Yin, H. Zhao and M. Lan, *Nanomedicine* **2025**.
[129] A. D. Korkmaz, *Materials Science and Engineering: B* **2023**, *295*, 116598.
[130] Y. Gao, X. D. Xie, F. Q. Li, Y. S. Lu, T. Li, S. Lian, Y. Y. Zhang, H. J. Zhang, H. Mei and L. Jia, *NANOSCALE* **2017**, *9*, 5624–5640.
[131] Z. Izadi, M. Rashidi, H. Derakhshankhah, M. Dolati, M. G. Kermanshahi, H. Adibi and H. Samadian, *RSC ADVANCES* **2023**, *13*, 34587–34597.
[132] A. P. Patil, P. A. Kamble, A. Pandey-Tiwari and U. V. Shembade, *BioNanoScience* **2024**.
[133] S. Bhattacharya, S. Bagade, P. C. Sangave, D. Kumar, I. Shaik and D. Mukherjee, *Biomacromolecules* **2024**, *25*, 7926–7950.
[134] X. Wan, Y. Zhang, Y. Wan, M. Xiong, A. Xie and Y. Liang, *ACS …* **2024**.
[135] H. Tabasi, M. H. Mosavian, Z. Sabouri, M. Khazaei and M. Darroudi, *Inorganic Chemistry Communications* **2021**, *125*, 108430.
[136] H. E. Alfassam, S. I. A. Othman and M. A. Al-Waili, *… Science, Part B* **2023**.
[137] M. Jahedi and A. Meshkini, *Colloids and Surfaces B: Biointerfaces* **2023**, *226*, 113333.
[138] Y. A. Hassan, M. Y. Alfaifi, A. A. Shati and S. E. I. Elbehairi, *Journal of Drug Delivery …* **2022**.
[139] H. Feng, M. Li, Z. Xing, X. Ouyang and J. Ling, *Journal of Drug Delivery Science …* **2022**.
[140] M. B. Uzun, S. Guderer, S. Banerjee and A. Yilmaz, *JOURNAL OF MOLECULAR STRUCTURE* **2025**, *1321*.
[141] J. Du, J. Liu, Z. Zhao, J. Dai, K. Li and Y. Lin, *ACS Applied Bio Materials* **2022**.
[142] B. Kumar, S. Kulanthaivel, A. Mondal, S. Mishra, B. Banerjee, A. Bhaumik, I. Banerjee and S. Giri, *COLLOIDS AND SURFACES B-BIOINTERFACES* **2017**, *150*, 352–361.
[143] F. Mahboubi, J. Mohammadnejad and S. Khaleghi, *Heliyon* **2024**.
[144] Q. Li, J. Liu, H. Fan, L. Shi, Y. Deng, L. Zhao, M. Xiang, Y. Xu, X. Jiang and G. Wang, *Biomaterials* **2021**, *269*, 120388.
[145] S. Bullo, K. Buskaran, R. Baby, D. Dorniani, S. Fakurazi and M. Z. Hussein, *Pharmaceutical Research* **2019**, *36*.
[146] D. Ge, D. Ren, Y. Duan, X. Luo, S. He and W. Qin, *Science China …* **2025**.
[147] H. P. Jiang, X. Y. Shi, X. Y. Yu, X. J. He, Y. H. An and H. J. Lu, *PHARMACEUTICAL RESEARCH* **2018**, *35*.
[148] K. AbouAitah, A. Stefanek, I. M. Higazy and M. Janczewska, *Pharmaceutics* **2020**.
[149] J. M. Jin, Y. J. Chen, H. Z. Li, Y. P. Xu and L. Y. Wang, *PHYSICAL CHEMISTRY CHEMICAL PHYSICS* **2024**, *26*, 23277–23287.
[150] J. C. Guo, S. H. Deng, S. M. Zhou, X. Zhou and J. Du, *RSC Medicinal …* **2024**.
[151] K. Rayappan, C. Murugan, S. Sundarraj, R. P. Lara and S. Kannan, *CHEMISTRYSELECT* **2017**, *2*, 8524–8534.
[152] D. Cai, C. Han, C. Liu, X. Ma, J. Qian, J. Zhou and Y. Li, *Nanoscale Research …* **2020**.
[153] H. Zhou, J. Yang, Z. Li, J. Feng, X. Duan, C. Yan, G. Wen, X. Qiu and Z. Shen, *Acta Biomaterialia* **2024**, *185*, 456–466.
[154] A. B. ÖztÜrk, N. Oğuz, H. T. Şahİn, S. Emik and E. Alarcin, *Turkish Journal of Chemistry* **2020**, *44*, 518–534.
[155] H. Xu, Z. Su, H. Zhang, Y. Zhang, Y. Bao and H. Zhang, *International Journal of …* **2023**.
[156] J. Tang, Y. Chen, H. Lai, Q. Zeng, Y. Li, J. Feng, N. Lin, R. Jin, J. Liu and T. Luo, *Chemical Engineering Journal* **2025**, 163582.
[157] Z. Zhang, L. Zhang, C. Huang, Q. Guo, Y. Zuo, N. Wang, X. Jin, L. Zhang and D. Zhu, *Biomaterials Science* **2020**, *8*, 6754–6763.
[158] J. Zhang, R. Fang, N. Song, Y. Jin and M. Zhang, *ACS Biomaterials …* **2025**.

[159] A. K. Meka, L. J. Jenkins, M. Dàvalos-Salas, N. Pujara, K. Y. Wong, T. Kumeria, J. M. Mariadason and A. Popat, *PHARMACEUTICS* **2018**, *10*.
[160] N. Summerlin, Z. Qu, N. Pujara, Y. Sheng, S. Jambhrunkar, M. McGuckin and A. Popat, *COLLOIDS AND SURFACES B-BIOINTERFACES* **2016**, *144*, 1–7.
[161] Y. Shen, L. Wang, B. Ji, X. Lu, D. Zhao and Y. Dai, *Chemical Engineering …* **2024**.
[162] K. Zarkesh, R. Heidari, P. Iranpour and N. Azarpira, *Journal of Drug Delivery …* **2022**.
[163] D. Zhang, X. He, Y. Wei, Q. Fan, J. Qiao, G. Jin and N. Li, *AIP Advances* **2024**, *14*.
[164] M. Guo, J. Ling, X. Xu and X. Ouyang, *International Journal of Molecular Sciences* **2023**, *24*, 6854.
[165] F. Farjadian, M. Moghadam and M. Monfared, *AIChE …* **2022**.
[166] B. Alallam, E. Abdkadir, A. Hayati and Y. Y. Keong, *Drug Delivery and …* **2025**.
[167] P. Singh, H. Singh, V. Castro-Aceituno, S. Ahn, Y. J. Kim, M. E. A. Farh and D. C. Yang, *Journal of Nanoparticle Research* **2017**, *19*.
[168] J. L. Andrade, C. A. Moreira and A. G. Oliveira, *Waste and biomass …* **2022**.
[169] S. Lahmadi, S. Alamery, A. Beagan, K. Alotaibi and A. Alswieleh, *RSC advances* **2024**, *14*, 8819–8828.
[170] J. C. F. Karnopp, J. Jorge, J. R. da Silva, D. Boldo, K. F. Del Pino Santos, A. P. Duarte, G. R. de Castro, R. B. de Azevedo, A. L. Prada and J. R. R. Amado, *Pharmaceutics* **2024**, *16*, 1086.
[171] K. AbouAitah, H. A. Hassan, A. Swiderska-Sroda, L. Gohar, O. G. Shaker, J. Wojnarowicz, A. Opalinska, J. Smalc-Koziorowska, S. Gierlotka and W. Lojkowski, *CANCERS* **2020**, *12*.
[172] J.-J. Shen, S.-J. Xue, Z.-H. Mei, T.-T. Li, H.-F. Li, X.-F. Zhuang and L.-M. Pan, *Heliyon* **2024**, *10*.
[173] A. H. Falemban, I. A. A. Ibrahim, G. A. Bamagous, A. R. Alzahrani, I. Shahid, N. Shahzad, S. H. Hussein-Al-Ali, P. Arulselvan and I. Thangavelu, *Inorganic Chemistry Communications* **2025**, *171*, 113517.
[174] Z. Khatibi, N. M. Kazemi and S. Khaleghi, *… Drug Delivery Science and Technology* **2022**.
[175] M. Pei, K. Liu, X. Qu, K. Wang, Q. Chen and Y. Zhang, *Journal of …* **2023**.
[176] A. D. Ayub, H. I. Chiu, S. N. A. Mat Yusuf, E. Abd Kadir, S. H. Ngalim and V. Lim, *Artificial Cells, Nanomedicine and Biotechnology* **2019**, *47*, 353–369.
[177] P. Sahoo, S. Kundu, S. Roy, S. Sharma, J. Ghosh, S. Mishra, A. Mukherjee and C. K. Ghosh, *RSC advances* **2022**, *12*, 24555–24570.
[178] Q. Liu, Y. Xiang, Q. Yu, Q. Lv and Z. Xiang, *Scientific reports* **2024**, *14*, 3328.
[179] H. Singh, J. PonnanEttiyappan and R. BalaKrishnan, *Colloids and Surfaces A: Physicochemical and Engineering Aspects* **2025**, *724*, 137390.
[180] B. T. Le, C. Q. Nguyen, P. T. Nguyen, H. D. Ninh and T. M. Le, *ACS …* **2022**.
[181] U.-C. N. Le, N. X. D. Mai, K.-M. Le, H. A. Vu, H.-N. T. Tran and T. L. H. Doan, *Arabian Journal of Chemistry* **2024**, *17*, 105402.
[182] R. Foroutan, A. Mohammadzadeh, S. Javanbakht, R. Mohammadi and M. Ghorbani, *RESULTS IN CHEMISTRY* **2025**, *15*.
[183] N. D. Thorat, J. Bauer, S. A. M. Tofail and V. G. Perez, *Colloids and Surfaces B …* **2020**.
[184] A. Abrishami, A. R. Bahrami, A. S. Saljooghi and M. M. Matin, *Nanoscale* **2024**, *16*, 6215–6240.
[185] Y. Hassanpouraghdam and M. Pooresmaeil, *International Journal of …* **2022**.
[186] S. Alavinia, R. Ghorbani-Vaghei, R. Haddadi, K. Sanemar, S. S. Uroomiye, A. Nourian and N. Emami, *International Journal of Biological Macromolecules* **2025**, *309*.
[187] S. Bhattacharyya and R. I. Fernandaes, *European Journal of Parenteral and Pharmaceutical Sciences* **2025**, *30*.

[188] L. Qiao, Y. Ou, L. Li, S. Wu, Y. Guo, M. Liu, D. Yu, Q. Chen, J. Yuan, C. Wei, C. Ou, H. Li, D. Cheng, Z. Yu and Z. Li, *Journal of Nanobiotechnology* **2024**, *22*.
[189] G. N. ghalee-taki, A. A. Rastegari, A. Hekmat and M. Rezaee, *BioNanoScience* **2024**.
[190] C. Cui, Z. Sun, Y. X. Gao and Q. Sun, *Journal of Nanoparticle Research* **2025**.
[191] N. Thirumalaivasan, P. Venkatesan, P. S. Lai and S. P. Wu, *ACS APPLIED BIO MATERIALS* **2019**, *2*, 3886–3896.
[192] Y. Li, J. Zhou, L. Wang and Z. Xie, *ACS applied materials &interfaces* **2020**.
[193] S. Iranpour, A. R. Bahrami and S. Nekooei, *Journal of …* **2021**.
[194] R. Mohammadi, A. Saboury, S. Javanbakht, R. Foroutan and A. Shaabani, *EUROPEAN POLYMER JOURNAL* **2021**, *153*.
[195] N. Vilaça, A. R. Bertão, E. A. Prasetyanto and S. Granja, *Materials Science and …* **2021**.
[196] M. Parsaei and K. Akhbari, *Inorganic Chemistry* **2022**.
[197] W. Liu, F. Wang, Y. Zhu, X. Li, X. Liu, J. Pang and W. Pan, *Molecules* **2018**, *23*.
[198] T. S. Anirudhan, V. C. Sekhar and S. S. Nair, *JOURNAL OF DRUG DELIVERY SCIENCE AND TECHNOLOGY* **2019**, *51*, 569–582.
[199] M. Babaei, A. Abrishami and S. Iranpour, *Drug Delivery and …* **2025**.
[200] T. Sun, R. Xia, J. Zhou, X. Zheng, S. Liu and Z. Xie, *Materials Chemistry Frontiers* **2020**, *4*, 2346–2356.
[201] Y. Zhou, S. Liu, C. Hu, L. Cai and M. Pang, *Journal of Materials Chemistry B* **2020**.
[202] S. Yamane, A. H. B. Yusri, P. Y. Chen, A. J. van der Vlies, A. B. Mabrouk, I. Fetzer and U. Hasegawa, *Macromolecular Bioscience* **2025**, *25*.
[203] G. Dalei, D. Jena and S. Das, *CARBOHYDRATE RESEARCH* **2024**, *545*.
[204] X. Jian, J. Xu, L. Yang, C. Zhao, J. Xu and Z. Gao, *Analytical …* **2020**.
[205] A. Hashemzadeh, F. Amerizadeh and F. Asgharzadeh, *Journal of Cluster …* **2022**.
[206] J. Chen, C. Wang, Z. Y. Zhu, F. Wang and J. Shang, *Journal of Solid State …* **2024**.
[207] C. Liu, F. Jiang, Z. Xing, L. Fan, Y. Li, S. Wang, J. Ling and X. K. Ouyang, *Pharmaceutics* **2022**, *14*.
[208] M. Gholami, A. Hekmat, M. Khazaei and M. Darroudi, *Journal of Materials Science: Materials in Medicine* **2022**, *33*, 26.
[209] S. Tehrani Nejad, R. Rahimi, M. Najafi and S. Rostamnia, *ACS Applied Materials & Interfaces* **2024**, *16*, 3162–3170.
[210] H. Nabipour and Y. Hu, *Chemical Papers* **2022**.
[211] W. J. Zhang, A. Babu, Y. Z. Yan, S. S. Park and N. J. Jo, *Journal of Porous …* **2023**.
[212] X. Sun, F. Li, L. Yuan, Z. Bing, X. Li and K. Yang, *Journal of Biomedical Materials Research - Part B Applied Biomaterials* **2024**, *112*.
[213] A. G. Abd-Elsatar, M. M. Farag, H. F. Youssef, S. A. Salih, M. M. Mounier and E. El-Meliegy, *PROGRESS IN BIOMATERIALS* **2019**, *8*, 101–113.
[214] K. Nagaraja, K. M. Rao, K. K. Rao and S. S. Han, *Colloids and Surfaces A: Physicochemical and Engineering Aspects* **2022**, *641*, 128456.
[215] S. Tarasi, A. Ramazani, A. Morsali, M. L. Hu, S. Ghafghazi, R. Tarasi and Y. Ahmadi, *INORGANIC CHEMISTRY* **2022**, *61*, 13125–13132.
[216] S. A. Johari, M. Sarkheil and S. Veisi, *Environmental Science and Pollution Research* **2021**, *28*, 56772–56781.
[217] N. Y. Chun, S.-N. Kim, Y. S. Choi and Y. B. Choy, *Journal of Industrial and Engineering Chemistry* **2020**, *84*, 290–296.
[218] S. K. Das, S. Mishra, K. D. Saha, D. Chandra, M. Hara, A. A. Mostafa and A. Bhaumik, *Molecules* **2022**, *27*, 7326.
[219] M. Soroushmanesh, M. Dinari and H. Jalali, *Results in Engineering* **2025**, 105919.

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