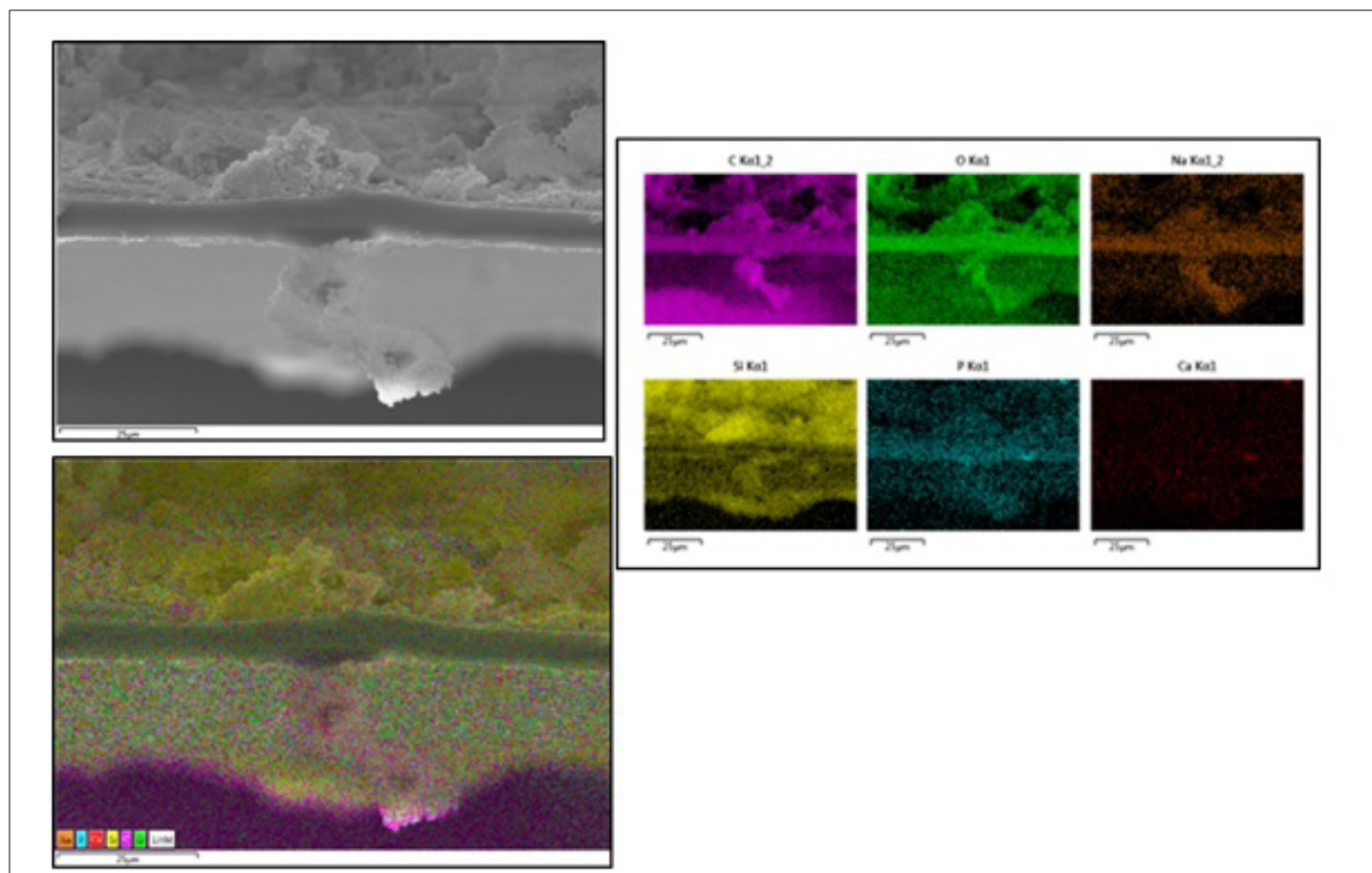


Molecularly Imprinted Polymer Nanostructure for Drug Stability and Binding Affinities in Biotherapeutics

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Received: 25-May-2026, Manuscript No. PAA-26-31672; **Editor assigned:** 27-May-2026, PreQC No. PAA-26-31672 (PQ); **Reviewed:** 10-Jun-2026, QC No. PAA-26-31672; **Revised:** 17-Jun-2026, Manuscript No. PAA-26-31672 (R); **Published:** 24-Jun-2026, DOI: 10.35248/2153-2435.25.17.844

Citation: Suedee R, Pholthien W, Prakannoppaku K, Kaewsud N, Santipiboon K, Getsuvan P. (2026). Molecularly Imprinted Polymer Nanostructure for Drug Stability and Binding Affinities in Biotherapeutics. Pharm Anal Acta. 17:844.

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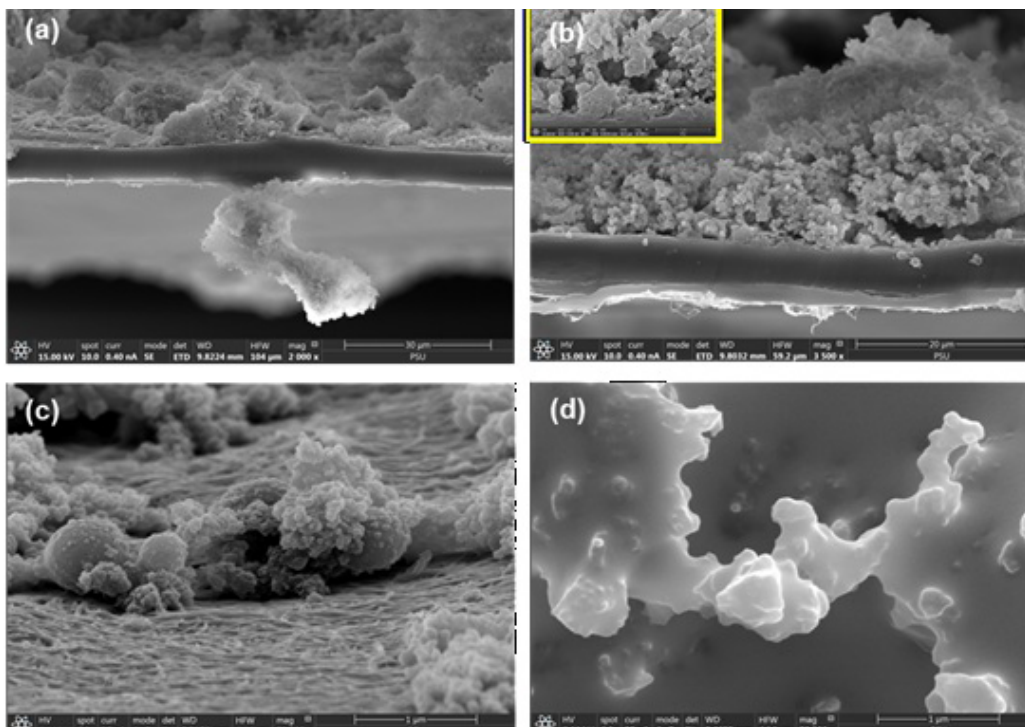


Figure S1: (Top panel) FE-SEM micrographs and EDX mapping of the compositional components remaining on the underlying bacterially derived cellulose membrane. Bottom panel: (a) and (b) cross-sectional views of the biocomposite, illustrating the cast layer and the impact of osmotic pinholes beneath it, along with the residual biocomposite component mixture.

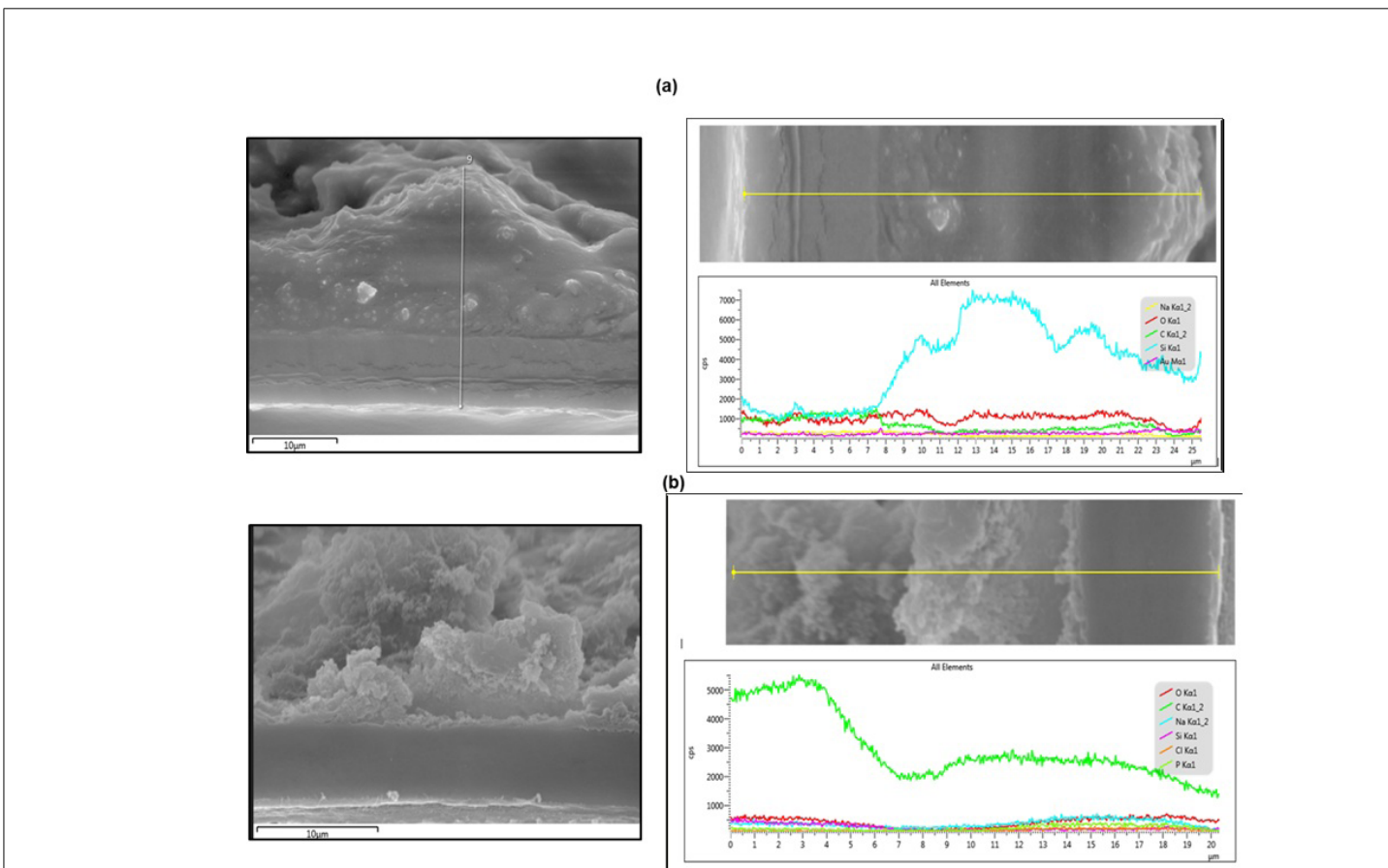


Figure S2: Panels (a) and (b) present top views of the cast layer, illustrating the residues and microspheres from the component mixture after its interaction with the octanol-aqueous layer at the porous surface of the membrane. These panels also display the line scan and X-ray dispersive binding energies corresponding to the elemental composition of the residual matrix resulting from the production process involving PCL-T gel over the nanofibril surface, alongside the osmosis flow through the natural cellulose membrane.

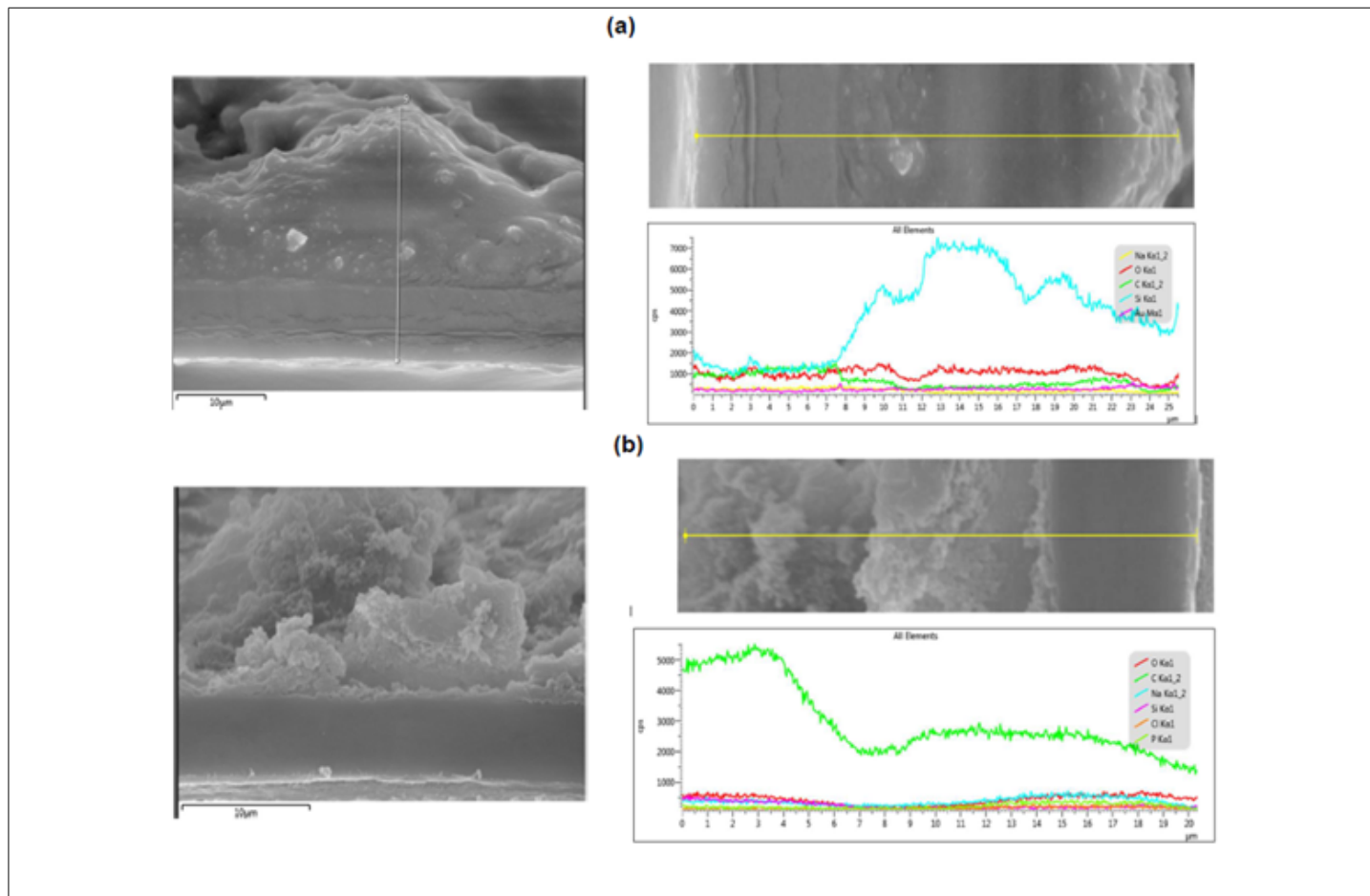
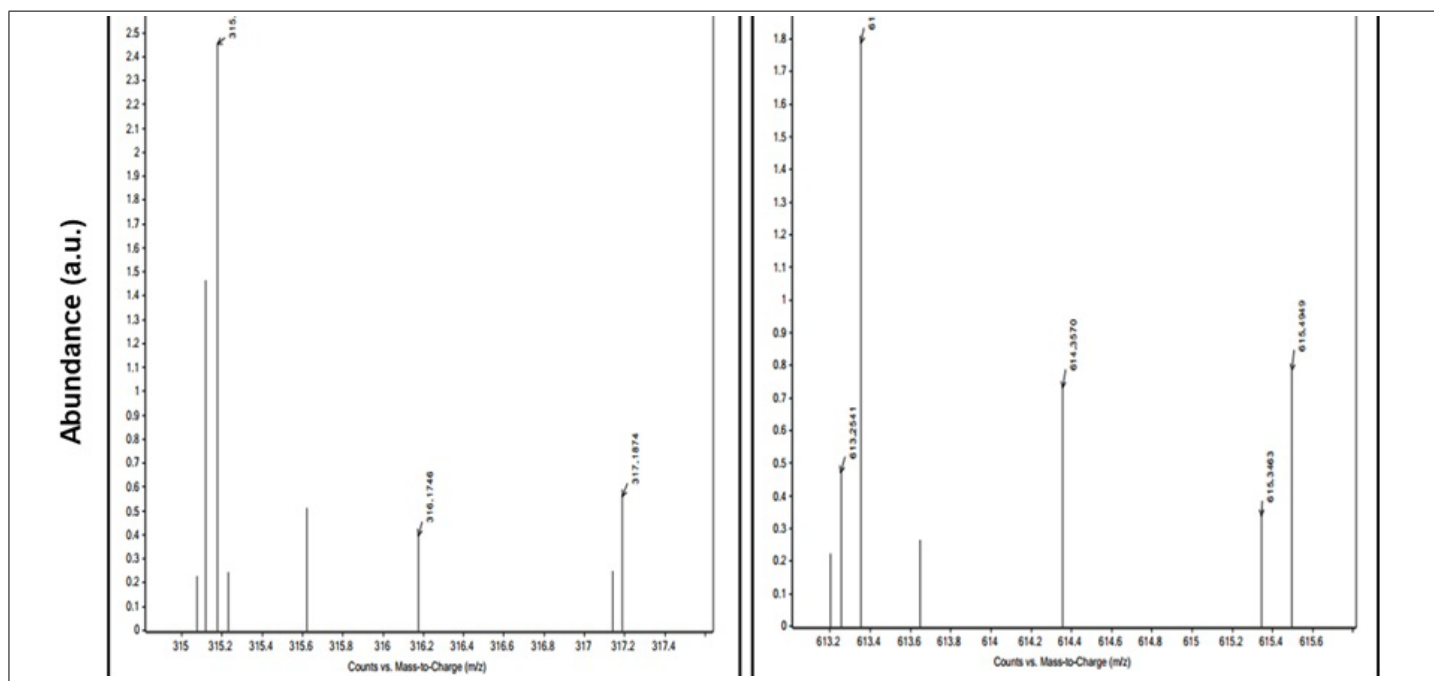
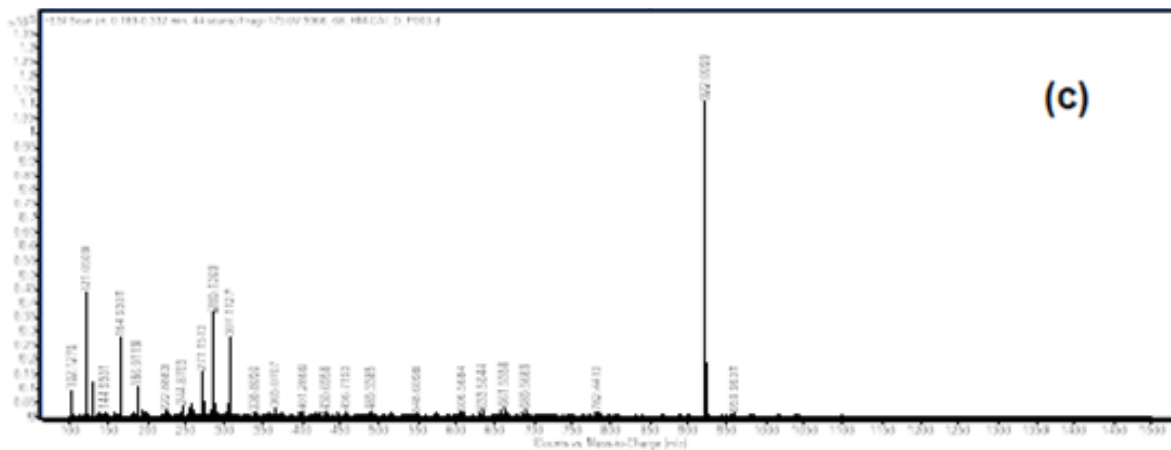


Figure S2: (A) left panel: SEM image of the drop-coated human serum albumin molecularly imprinted polymer (HSA-MIP) containing Cannabidiol (CBD), referred as MIP-C. The contact angle of HSA-MIP is assessed in both phosphate-buffered saline (PBS) and octanol.





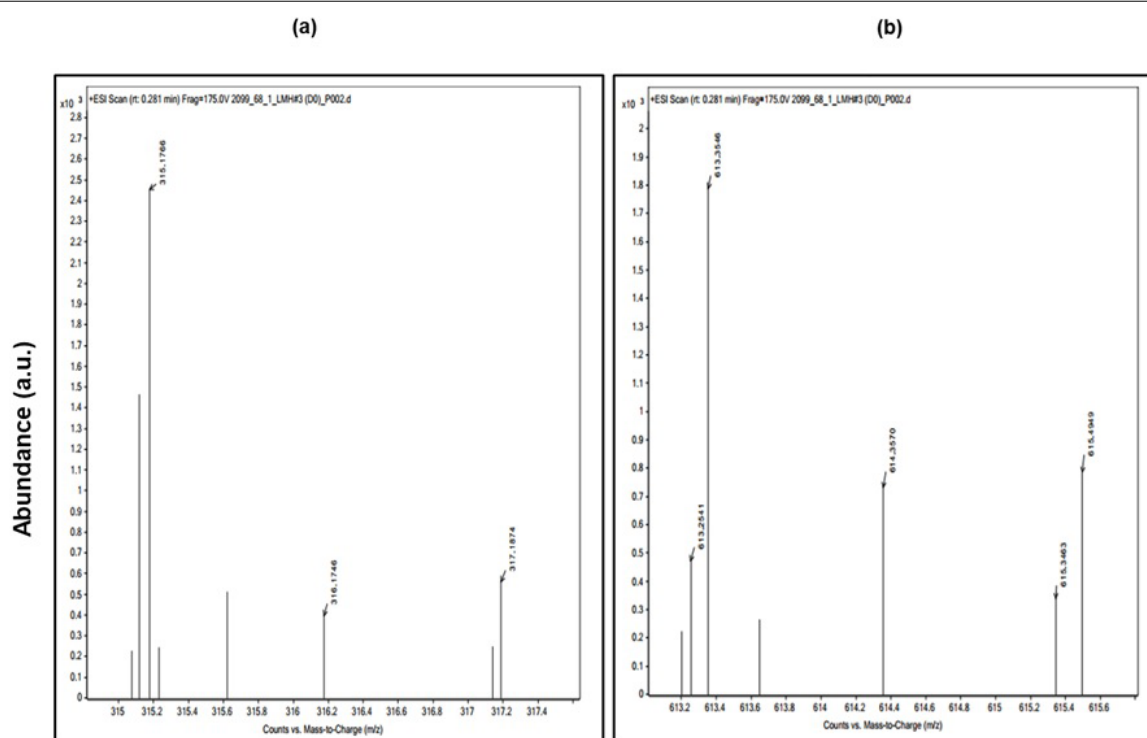


Figure S5: The high-resolution LC-QTOF (MS-ESI+) analysis of the buffered lysate layer from the filtrate recycling of CCF type IMN during Franz diffusion at room temperature.

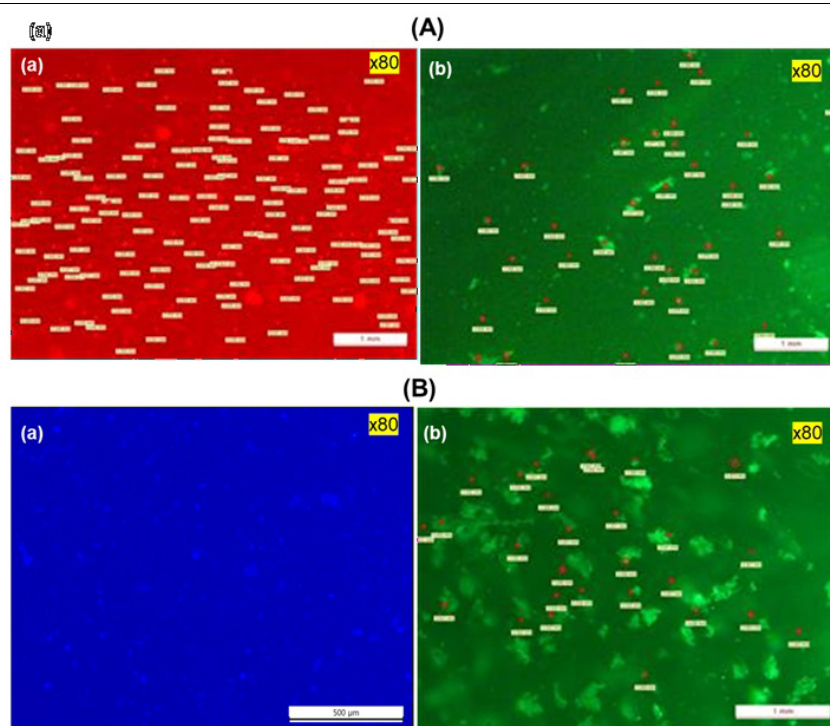


Figure S6: Microsystem analysis coupled fluorescence microscopy imaging in concert with Artificial Intelligence (AI) and convolutional neural networks (CNN), showing the biocomposite nanoparticles prepared from the customized drug blend formulation with clusters of IMN solution interfacing with a buffer (pH 7.4-7.5) (A) or (B) water (Freezing IMN), after storage for six months at ambient temperature, revealing variable fluorescence emissions.

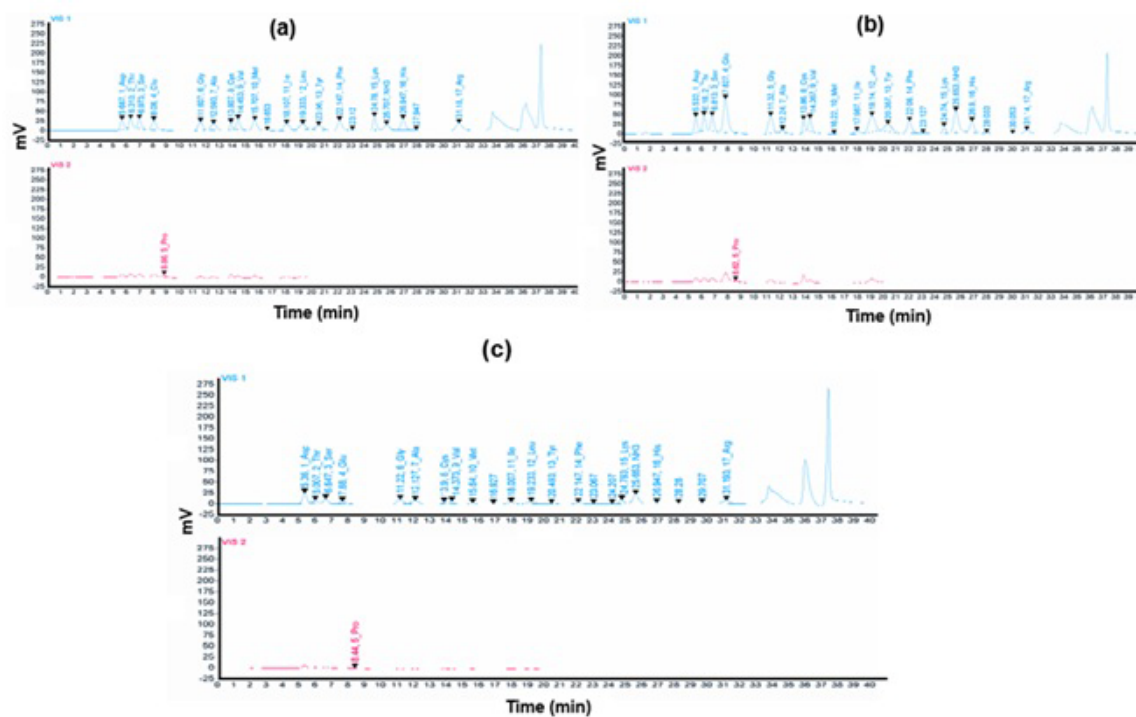


Figure S7: The amino acid analysis included the monoclonal antibody against IgE from IgG serum (a), insulin (b), and lysozyme used in this study (c).

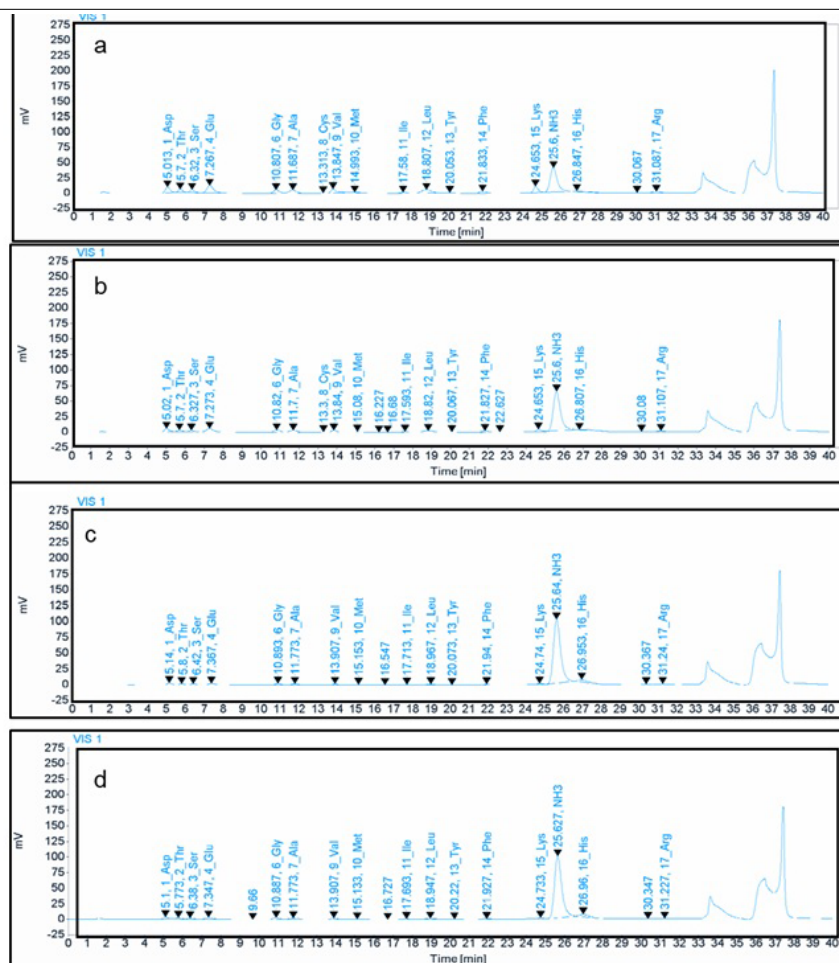


Figure S8: Amino acid concentration changes in the albumin nanocapsule MIP, across aging medium and filtrate, affected by CBD loading and processing after Franz diffusion for ISL type (a,c) and different CBD concentrations (b,d).

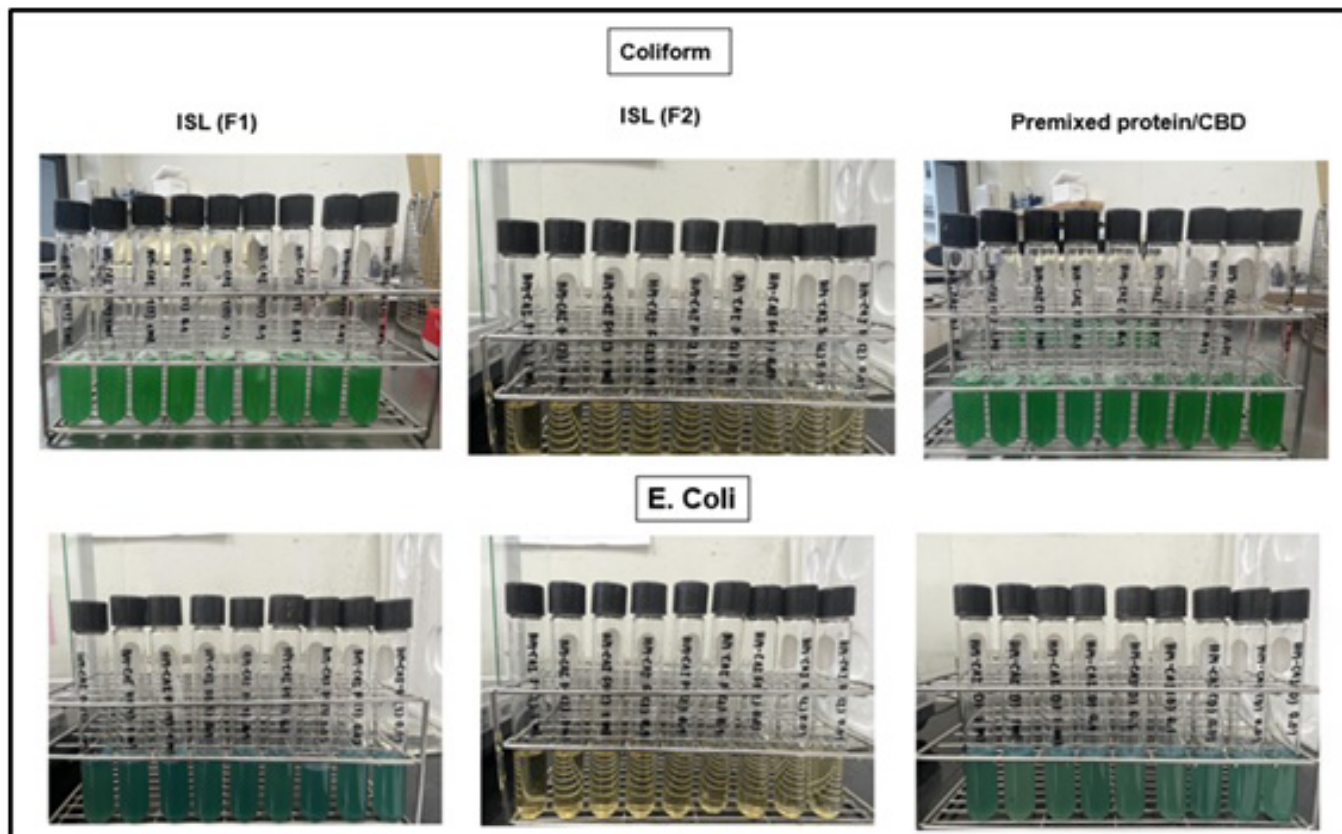


Figure S9: Microbiological evaluations of nanofiltration lysates tested from the ISL type of IMN.

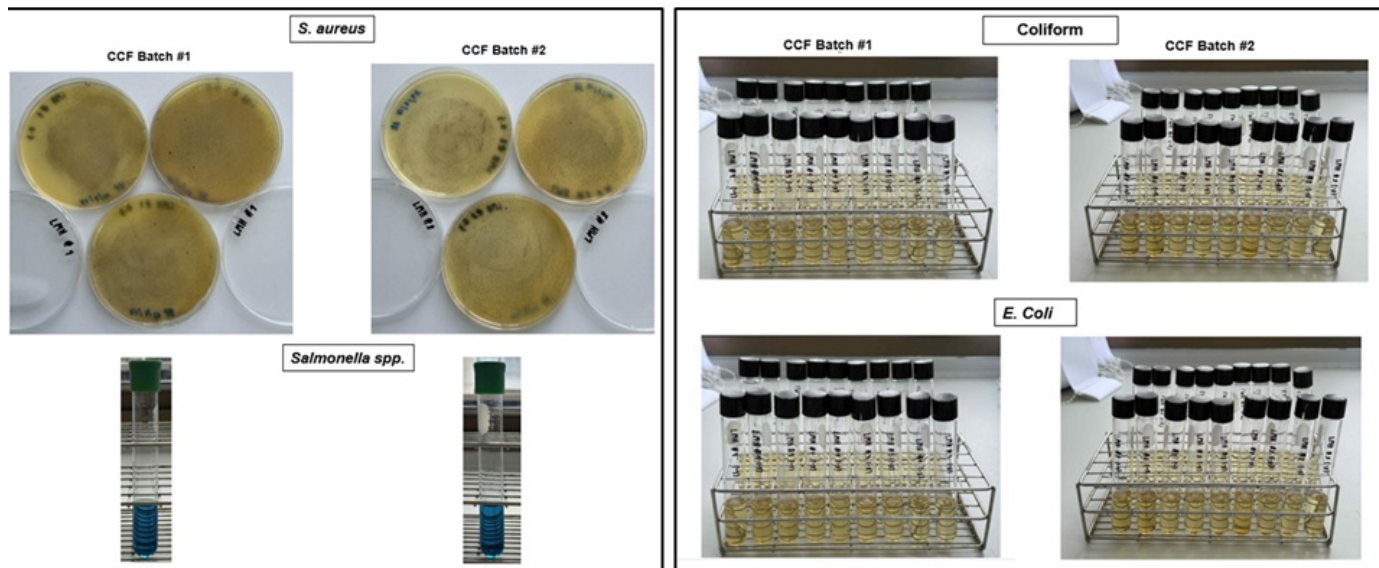


Figure S10: Microbiological evaluations of nanofiltration lysates tested from the CCF type of IMN.

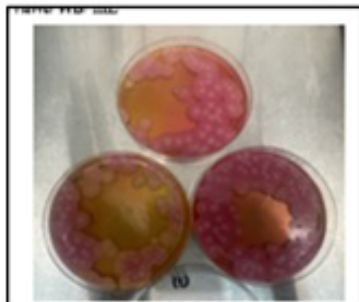
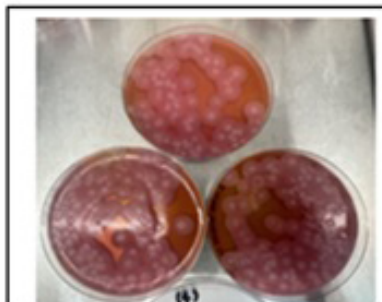
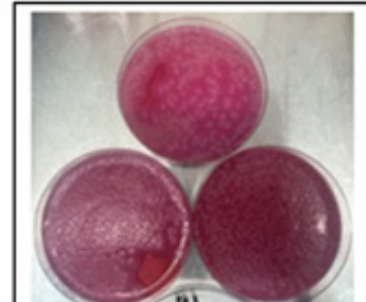
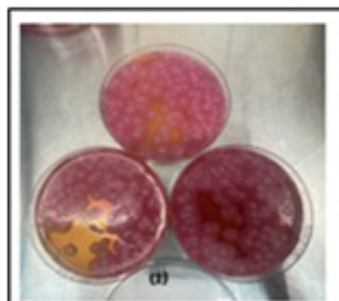
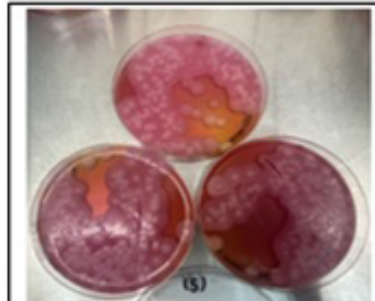
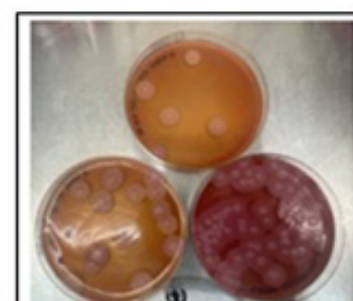
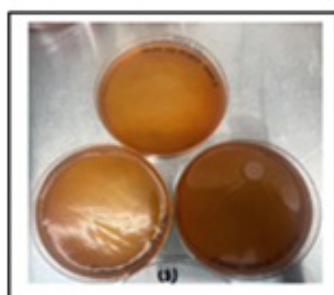
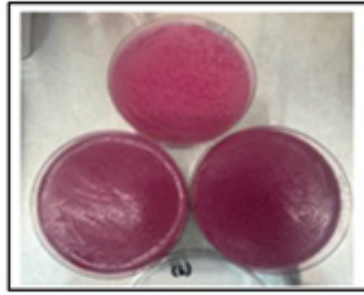
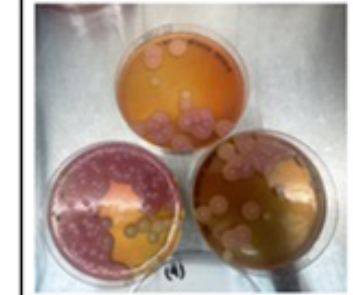
Bacillus cereus
testing**Sample CCF-1****Sample CCF-4****Sample CCF-7****Sample CCF-2****Sample CCF-5****Sample CCF-8****Sample CCF-3****Sample CCF-6****Sample CCF-9**

Figure S11: Microbial evaluation for the enumeration of *Bacillus cereus*, in accordance with BP 2025 guidelines. The lysates were reconstituted with 1 mL of sterile deionized water for each of the nine independent bioproduction runs conducted on a natural cellulose membrane, utilizing nanofiltration lysates derived from the CCF type of IMN after lyophilization.

Bacillus cereus testing

Sample CCF



Sample ISL

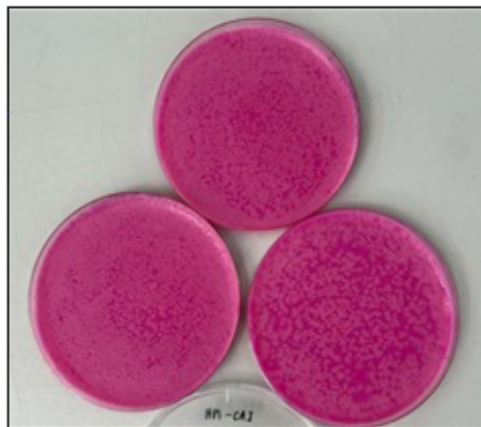


Figure S13: FT-IR spectra of the masked IMN after BET analysis, showing residues from ISL and CCF.

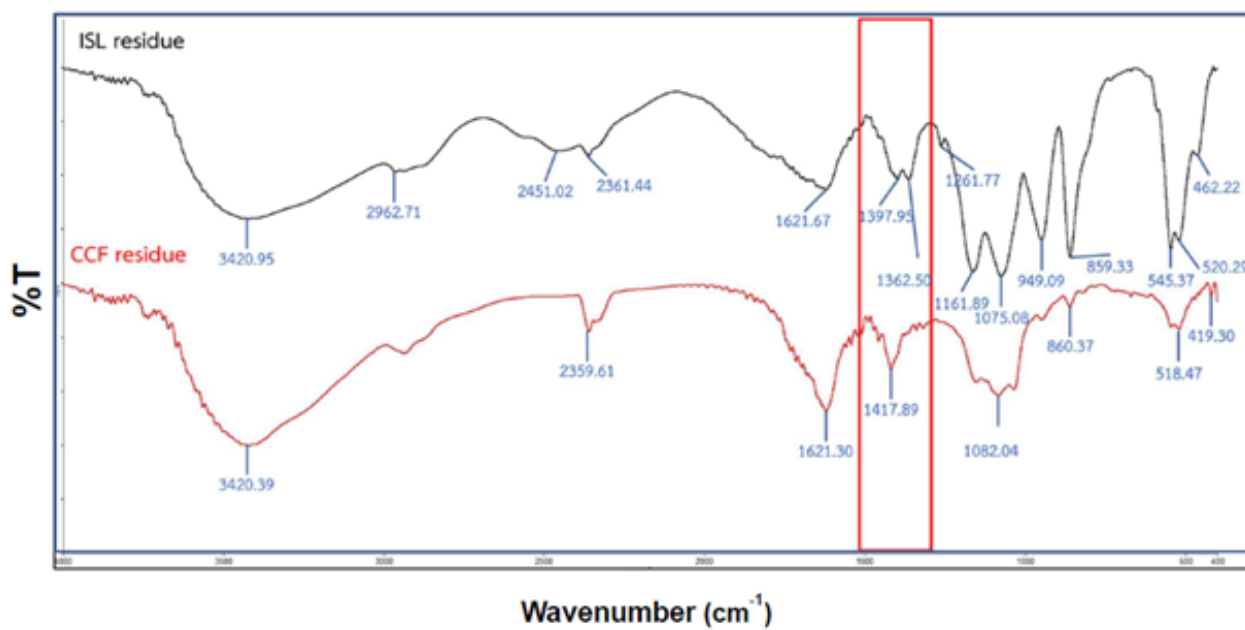


Figure S13: FT-IR spectra of the masked IMN after BET analysis, showing residues from ISL and CCF.

Table S1: Microbial analysis conducted with inoculum levels of 0.1 g, 0.01 g, and 0.001 g. The Most Probable Numbers (MPNs) per gram derived from the drug product of ISL type of IMN, across various batches and processing stages; means with associated 95% confidence intervals, based on a sample size of N=3.

e			MPN/g	Conf. lim.		Pos. Tubes			MPN/g	Conf. lim.	
0.1g	0.01g	0.001g		Low	High	0.1g	0.01g	0.001g		Low	High
	0	0	<3.0		9.5	2	2	0	21	4.5	42
0	0	1	3	0.15	9.6	2	2	1	28	8.7	94
0	1	0	3	0.15	11	2	2	2	35	8.7	94
0	1	1	6.1	1.2	18	2	3	0	29	8.7	94
0	2	0	6.2	1.2	18	2	3	1	36	8.7	94
0	3	0	9.4	3.6	38	3	0	0	23	4.6	94
0	0	0	3.6	0.17	18	3	0	1	38	8.7	110
1	0	1	7.2	1.3	18	3	0	2	64	17	180
1	0	2	11	3.6	38	3	1	0	43	9	180
1	1	0	7.4	1.3	20	3	1	1	75	17	200
1	1	1	11	3.6	38	3	1	2	120	37	420
1	2	0	11	3.6	42	3	1	3	160	40	420
1	2	1	15	4.5	42	3	2	0	93	18	420
1	3	0	16	4.5	42	3	2	1	150	37	420
1	0	0	9.2	1.4	38	3	2	2	210	40	430
2	0	1	14	3.6	42	3	2	3	290	90	1000
2	0	2	20	4.5	42	3	3	0	240	42	1000
2	1	0	15	3.7	42	3	3	1	460	90	2000
2	1	1	20	4.5	42	3	3	2	1100	180	4100
2	1	2	27	8.7	94	3	3	3	>1000	420	

Table S2: Microbial analysis from the drug product of CCF type of IMN, across various batches; means with associated 95% confidence intervals, based on a sample size of N=3.

Pos. Tubes			MPN/g	Conf. Lim		Pos. Tubes			MPN/g	Conf. Lim	
0.1	0.01	0.001		Low	High	0.1	0.01	0.001		Low	High
0	0	0	<3.0	-	9.5	2	2	0	21	4.5	42
0	0	1	3	0.15	9.6	2	2	1	28	8.7	94
0	1	0	3	0.15	11	2	2	2	35	8.7	94
0	1	1	6.1	1.2	18	2	3	0	29	8.7	94
0	2	0	6.2	1.2	18	2	3	1	36	8.7	94
0	3	0	9.4	3.6	38	3	0	0	23	4.6	94
1	0	0	3.6	0.17	18	3	0	1	38	8.7	110
1	0	1	7.2	1.3	18	3	0	2	64	17	180
1	0	2	11	3.6	38	3	1	0	43	9	180
1	1	0	7.4	1.3	20	3	1	1	75	17	200
1	1	1	11	3.6	38	3	1	2	120	37	420
1	2	0	11	3.6	42	3	1	3	160	40	420
1	2	1	15	4.5	42	3	2	0	93	18	420
1	3	0	16	4.5	42	3	2	1	150	37	420
2	0	0	9.2	1.4	38	3	2	2	210	40	430

2	0	1	14	3.6	42	3	2	3	290	90	1,000
2	0	2	20	4.5	42	3	3	0	240	42	1,000
2	1	0	15	3.7	42	3	3	1	460	90	2,000
2	1	1	20	4.5	42	3	3	2	1100	180	4,100
2	1	2	27	8.7	94	3	3	3	>1100	420	-

Table S3: Evaluation of *Bacillus cereus* using nanofiltration lysates derived from the CCF type of IMN following the guidelines of BP 2025. The lysates were reconstituted with 1 mL of sterile deionized water, and samples were collected from nine independent runs of the bioproduction process carried out on a natural cellulose membrane.

Run info:
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 Comment:
 Operator: tof-user@FLEX-PC
 Run creation Date/Time: 2026-03-26T14:58:41.056
 Number of Tests: 25
 Type: Standard
 BTS-QC: Not presented
 BTS-QC Position:
 Instrument ID: 8269944.03836
 Server Version: 4.1.80 (PYTH) 102 2017-08-226_04-55-52



Sample name	Sample ID	Organism (best match)	Score value	Organism (second best match)	Score value
B1 (+++) A	C_B.cereus-(1)-1 (standard)	Bacillus cereus	2.07	Bacillus cereus	1.96
B2 (+) B	C_B.cereus-(1)-2 (standard)	Bacillus cereus	1.98	Bacillus cereus	1.89
B3 (+++) A	C_B.cereus-(1)-3 (standard)	Bacillus cereus	2.3	Bacillus cereus	2.15
B4 (+) B	C_B.cereus-(2)-1 (standard)	Bacillus cereus	2.1	Bacillus cereus	2.08
B5 (+++) A	C_B.cereus-(2)-2 (standard)	Bacillus cereus	2.32	Bacillus cereus	2.13
B6 (+++) A	C_B.cereus-(2)-3 (standard)	Bacillus cereus	2.42	Bacillus cereus	2.42
B7 (+++) A	C_B.cereus-(3) (standard)	Bacillus cereus	2.11	Bacillus cereus	2.09
B8 (+++) A	C_B.cereus-(4)-1 (standard)	Bacillus cereus	2.29	Bacillus cereus	2.2
B9 (+++) A	C_B.cereus-(4)-2 (standard)	Bacillus cereus	2.26	Bacillus cereus	2.23
B10 (+++) A	C_B.cereus-(4)-3 (standard)	Bacillus cereus	2.2	Bacillus cereus	2.18
B11 (+++) A	C_B.cereus-(5)-1 (standard)	Bacillus cereus	2.33	Bacillus cereus	2.32
B12 (+++) A	C_B.cereus-(5)-2 (standard)	Bacillus cereus	2.16	Bacillus cereus	2.02
C1 (+++) A	C_B.cereus-(5)-3 (standard)	Bacillus cereus	2.22	Bacillus cereus	2.21
C2 (+++) A	C_B.cereus-(6)-1 (standard)	Bacillus cereus	2.26	Bacillus cereus	2.23
C3 (+++) A	C_B.cereus-(6)-2 (standard)	Bacillus cereus	2.24	Bacillus cereus	2.21
C4 (+++) A	C_B.cereus-(6)-3 (standard)	Bacillus cereus	2.15	Bacillus cereus	2.13
C5 (+++) A	C_B.cereus-(7)-1 (standard)	Bacillus cereus	2.12	Bacillus cereus	2.09
C6 (+++) A	C_B.cereus-(7)-2 (standard)	Bacillus cereus	2.3	Bacillus cereus	2.25

Meaning of score values

Range	Interpretation	Symbols	Color
2.00-3.00	High-confidence identification	(+++)	Green
1.70-1.99	Low-confidence identification	(+)	Yellow
0.00-1.69	No organism identification possible	(-)	Red

Table S4: A microbial enumeration of *Bacillus cereus* based on nanofiltration lysates obtained from two different types of IMN: The CCF type, referred to as LMH, and the ISL type, designated as HM-CAI, following the lyophilization process. The accompanying panel analyzes the meaning score for *Bacillus cereus*, which assists in interpretation.

Run Info:
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 Number of Tests: 5
 Type: Standard
 BTS-QC: Not presented
 BTS-QC Position:
 Instrument ID: 8269944.03836
 Server Version: 4.1.80 (PYTH) 102 2017-08-226_04-55-52



Sample name	Sample ID	Organism (best match)	Score value	Organism (second best match)	Score value
D9 (+++) A	LMH#3_1 (standard)	Bacillus cereus	2.26	Bacillus cereus	2.1
D10 (+++) A	LMH#3_2 (standard)	Bacillus cereus	2.29	Bacillus cereus	2.16
D11 (+++) A	HM-CAI_1 (standard)	Bacillus cereus	2.23	Bacillus cereus	2.22
D12 (+) B	HM-CAI_1 (standard)	Bacillus cereus	1.97	Bacillus cereus	1.97
H9 (+++) A	BTS (BTS)	Bacillus cereus	2.05	Bacillus cereus	2.03

Meaning of score values

Range	Interpretation	Symbols	Color
2.00-1.00	High-confidence identification	(+++)	Green
1.70-1.99	Low-confidence identification	(+)	Yellow
0.00-1.69	No organism identification possible	(-)	Red

Table S5: A verification of *Bacillus cereus* identification utilizing nanofiltration lysates obtained from the ISL variant of the IMN (designated as HM-CAI) post-lyophilization. The corresponding panel displays the average score for *Bacillus cereus*, indicating a notable inconsistency in the results, with several yielding non-confident outcomes.

Run Info:
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 Type: Standard
 BTS-QC: Not presented
 BTS-QC Position:
 Instrument ID: 8269944.038
 Server Version: 4.1.80 (PYTH) 102 2017-08-226_04-55-52



Sample Name	Sample ID	Organism (best match)	Score Value	Organism (second best match)	Score Value
D12 (+) (B)	HM-CAI_2 (Standard)	Bacillus cereus	1.98	Bacillus cereus	1.84

Meaning of score values

Range	Interpretation	Symbols	Color
2.00-3.00	High-confidence identification	(+++)	Green
1.70-1.99	Low-confidence identification	(+)	Yellow
0.00-1.69	No organism identification possible	(-)	Red

Table S4: A microbial enumeration of *Bacillus cereus* based on nanofiltration lysates obtained from two different types of IMN: The CCF type, referred to as LMH, and the ISL type, designated as HM-CAI, following the lyophilization process. The accompanying panel analyzes the meaning score for *Bacillus cereus*, which assists in interpretation.

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 Sample description:
 Sample ID: BTS
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 Preprocessing method: MALDI Biotyper preprocessing standard method 1.1
 ACQ method D: \Methods\flexControl\Methods\MBT_FC.par
 ACQ Timestop: 2026-04-10T09:14:19.997
 AutoXecute method: MBT_AutoX
 Applied MSP Library (ies): BDAI./contains 10833 MSPa/cb2dd1f0-1dc2-4fc0-83b7-83aa0cab5c76/2022-06-16T22:36c25.726



Rank (Quality)	Matched pattern	Score value	NCBI Identifier
1 (+)	Escherichia coli MB11464 1 CHB	1.86	562
2 (+)	Escherichia coli ATCC 35218 CHB	1.76	562
3 (+)	Escherichia coli DSM 682 DSM	1.74	562
4 (+)	Escherichia coli DSM 1576 DSM	1.73	562
5 (+)	Escherichia coli ATCC 25922 THL	1.72	562
6 (+)	Escherichia coli DHSalpha BRL	1.72	562
7 (-)	Escherichia coli DSM 1103_QC DSM	1.66	562
8 (-)	Escherichia coli DSM 30083T HAM	1.66	562
9 (-)	Escherichia coli ATCC 25922 CHB	1.66	562
10 (-)	Escherichia coli Nissl VML	1.63	562

Meaning of score values

Range	Interpretation	Symbols	Color
2.00-1.00	High-confidence identification	(+++)	Green
1.70-1.99	Low-confidence identification	(+)	Yellow
0.00-1.69	No organism identification possible	(-)	Red