Electronic Supplementary Material (ESI) for Environmental Science: Nano.

Cytotoxicity Analysis of Nanoparticles by Association Rule Mining

SUPPLEMENTARY INFORMATION

S1. Additional Information on Computational Method

S1.1. Data Set Construction

- The comprehensive NP toxicity dataset including all feature descriptors are given in a separate Excel sheet.

S1.2. Computational Details

- For association rule mining, the data set was categorized into three classes as low (≤ 50%), medium (50-85), and high (≥85%) viability of cells.
- The discretization was carried out for diameter, concentration, PDI, and aspect ratio variables. Their minimum, maximum and mean values in the data set are listed in Table S1.1. The PDI values were discretized into five intervals with *equal-width binning* approach since their range is in between 0 to 1. The bins consist of the ranges of [0-0.2], (0.2-0.4], (0.4-0.6], (0.6-0.8] and (0.8-1.0]. Since aspect ratio values cover a wide spectrum, they were discretized with *equal-width binning* approach but in the logarithmic scale as (0-1), [1-2), [2-3) and above 3. Similarly, concentration values were split into five bins in the logarithmic scale as (0-1), [1-2), [2-3), [3-4) and above 4. Here, values from 0 to 10 fall into the first range, values from 10 to 100 fall into the second range, values from 100 to 1000 fall into the third range, and so on. Then considering our sample numbers, we narrowed the third interval from 100 to 200 and similar results were found. In the manuscript the results based on these ranges were presented.

Table S1.1. The statistical descriptors of continuous numerical data.

	Min	**Max**	**Mean**
Diameter (nm)	1.15	500	47.3
Concentration (μg/ml)	0.001	14015.2	152.8
PDI	0.005	1.0	0.33
Aspect Ratio	0.1	3333	155.2

As to diameter, two procedures were followed. First, the range of diameter values was discretized into five bins of 25 nm width. However, these intervals did not differentiate from each other in terms of significance for single factor association including diameter and viability. On the other hand, when we combined material and diameter, significant associations were obtained and listed in Table S1.2.

Table S1.2. Material, diameter, and viability association with equal-width binning of diameter.

Material & Diameter Association				
Antecedent → Consequent	**Support**	**Confidence**	**Lift**	**Count**
{Material = HAP, Diameter = (0, 25] nm → High Viability}	0.010	1.0	1.95	24*
{Material = Polystyrene, Diameter = (75, 100] nm → High Viability}	0.016	0.84	1.64	37
{Material = Titanium oxide, Diameter = (0, 25] nm → High Viability}	0.017	0.80	1.56	40
{Material = Iron oxide, Diameter = (0, 25] nm → High Viability}	0.032	0.80	1.56	75
{Material = Cerium oxide, Diameter = (0, 25] nm → High Viability}	0.012	0.78	1.53	29
{Material = Eudragit RL, Diameter > 100 nm → High Viability}	0.012	0.78	1.52	28*
{Material = Iron oxide, Diameter = (25, 50] nm → High Viability}	0.011	0.75	1.46	27
{Material = MWCNT,	0.021	0.70	1.36	49

Diameter = (0, 25] nm → High Viability}

In literature the nanoparticles smaller than 10 nm have been shown to have more potential to be toxic.[1] Therefore, we changed our discretization technique to present whether this hypothesis is true or not. In our approach, discretization was performed using min-max and mean values based on reported cellular internalization of nanoparticles. The range of diameter values was divided into five intervals with the labels of extra-small (XS), small (S), medium (M), large (L) and extra-large (XL). It has been reported that NPs having a size <200 nm can be internalized by clathrin- or caveolin- mediated endocytosis,[2] while caveolin-mediated endocytosis inhibits the uptake of larger particles (>100nm).[3] Moreover, several studies reported an optimal size of 50 nm for NP internalization, while smaller size (~25 nm) NP internalization has been shown to decrease.[4] Hence, we took this information into account while discretizing our size data. Moreover, we separated 10 nm and smaller sized particles into a bin to measure their toxic effects. We obtained similar results (Table 2) with this discretization and had chance to reflect the effect of narrow ranges of 0-10 and 10-25 nm in the manuscript.

Table S1.3. Discretization of the diameter of nanoparticles.

Method	XS	S	M	L	XL
Equal width	(0 - 25] nm	(25 - 50] nm	(50 - 75] nm	(75 - 100] nm	100 <
Our approach	(0 - 10] nm	(10, 25] nm	(25-100] nm	(100-200]	200 <

It should be noted that the reader can easily determine different intervals with different discretization technique and can observe its effect since we provide both the data set and Python code.

S2. Additional Results

- The Association Rule Mining (ARM) results to investigate the cases which result in high cellular viability are provided as full lists (above lift of 1) in Table S2.1 and Table S2.2.

Table S2.1. Single factor associations resulting in high viability (≥ 85%). The associations were listed based on their ranked lift values (above 1).

Antecedent → Consequent	Support	Confidence	Lift	Count
{Material = HAP → High Viability}	0.020	0.94	1.83	46
{Material = Chitosan → High Viability}	0.014	0.85	1.66	34
{Material = Ceria → High Viability}	0.015	0.81	1.59	35
{Material = Eudragit RL→ High Viability}	0.012	0.78	1.52	28
{Material = PLGA → High Viability}	0.020	0.74	1.45	46
{Material = Iron oxide → High Viability}	0.052	0.72	1.40	122
{Material = Polystyrene → High Viability}	0.038	0.71	1.39	90
{Material = Titanium oxide → High Viability}	0.025	0.70	1.36	60
{Material = Dendrimer → High Viability}	0.014	0.69	1.34	33
{Material = MWCNT → High Viability}	0.031	0.65	1.26	73
{Material = Bismuth → High Viability}	0.013	0.55	1.08	31
{Material Type = Organic NPs → High Viability}	0.113	0.65	1.27	267
{Material Type = Carbon NPs → High Viability}	0.056	0.52	1.01	133
{Coat = Silica → High Viability}	0.013	0.73	1.43	30
{Coat = COOH → High Viability}	0.024	0.73	1.42	57
{Coat = Dextran → High Viability}	0.014	0.60	1.16	34
{Coat = PEG → High Viability}	0.025	0.58	1.13	58
{Coat = Citrate → High Viability}	0.026	0.54	1.04	61
{Coat = NH_2 → High Viability}	0.015	0.52	1.02	36
{Synthesis = Reverse Microemulsion → High Viability}	0.017	1.00	1.95	40
{Synthesis = Ionotropic Gelation → High Viability}	0.014	0.97	1.90	34
{Synthesis = Emulsion-Solvent Evaporation → High Viability}	0.028	0.66	1.29	67
{Synthesis = Precipitation → High Viability}	0.049	0.63	1.24	115
{Synthesis = Chemical Vapor Deposition → High	0.022	0.62	1.21	52

Viability}				
{Shape = Irregular → High Viability}	0.030	0.72	1.40	71
{Shape = Nanotube → High Viability}	0.037	0.54	1.05	88
{Shape = Rod → High Viability}	0.036	0.53	1.03	86
{Surface Charge = Neutral → High Viability}	0.012	1.00	1.95	29
{Surface Charge = Positive → High Viability}	0.092	0.52	1.01	216
{Surface Charge = Negative → High Viability}	0.274	0.52	1.01	644
{Concentration < 10 μg/ml → High Viability}	0.172	0.72	1.40	406
{Diameter ≤ 10 nm → High Viability}	0.084	0.56	1.08	199
{Diameter = (10, 25] nm → High Viability}	0.142	0.54	1.06	335
{Aspect Ratio = [10, 100) → High Viability}	0.036	0.69	1.35	86
{PDI = (0.8, 1] → High Viability}	0.012	0.66	1.29	29
{PDI = [0, 0.2] → High Viability}	0.074	0.64	1.24	173
{PDI = (0.2, 0.4] → High Viability}	0.032	0.52	1.01	75
{Cell Line/Primary Cells = Primary Cells → High Viability}	0.127	0.64	1.25	299
{Cell Type = MBMC → High Viability}	0.014	0.97	1.90	34*
{Cell Type = SIRC → High Viability}	0.010	0.83	1.62	25*
{Cell Type = SHSY5Y → High Viability}	0.020	0.78	1.53	47
{Cell Type = HCMEC → High Viability}	0.017	0.74	1.44	40*
{Cell Type = HUVEC → High Viability}	0.039	0.73	1.43	91
{Cell Type = PC12 → High Viability}	0.016	0.72	1.40	38
{Cell Type = L929 → High Viability}	0.018	0.71	1.39	42
{Cell Type = J774A.1 → High Viability}	0.014	0.67	1.31	33
{Cell Type = CCL-110 → High Viability}	0.011	0.63	1.24	26
{Cell Type = MG-63 → High Viability}	0.018	0.63	1.22	42
{Cell Type = RAW264.7 → High Viability}	0.012	0.57	1.11	29
{Cell Type = THP-1 → High Viability}	0.012	0.54	1.05	29
{Cell Source = Rabbit → High Viability}	0.011	0.83	1.62	25
{Cell Source = Mouse → High Viability}	0.082	0.55	1.08	194
{Cell Source = Hamster → High Viability}	0.012	0.54	1.05	29
{Cell Tissue = Cornea → High Viability}	0.011	0.83	1.62	25
{Cell Tissue = Heart → High Viability}	0.017	0.74	1.44	40
{Cell Tissue = Umbilical Vein → High Viability}	0.039	0.73	1.43	91

{Cell Tissue = Bone Marrow → High Viability}	0.042	0.72	1.41	99
{Cell Tissue = Adrenal Gland → High Viability}	0.016	0.72	1.40	38
{Cell Tissue = Subcutaneous Connective Tissue → High Viability}	0.018	0.71	1.39	42
{Cell Tissue = Ascites → High Viability}	0.026	0.62	1.21	62
{Cell Tissue = Bone → High Viability}	0.032	0.60	1.17	76
{Cell Tissue = Ovary → High Viability}	0.011	0.52	1.02	25
{Cell Morphology = Spindle → High Viability}	0.021	0.77	1.50	50
{Cell Morphology = Endothelial → High Viability}	0.042	0.73	1.43	99
{Cell Morphology = Irregular → High Viability}	0.016	0.72	1.40	38
{Cell Morphology = Monocyte → High Viability}	0.014	0.57	1.11	33
{Cell Morphology = Monocyte/Macrophage → High Viability}	0.012	0.57	1.11	29
{Cell Age = Fetus → High Viability}	0.018	0.60	1.18	43
{Cell Age = Embryonic → High Viability}	0.068	0.55	1.07	159
{Animal/Human Cells = Animal → High Viability}	0.146	0.52	1.02	343
{Test = CCK-8 → High Viability}	0.082	0.65	1.27	193
{Test = MTS → High Viability}	0.069	0.62	1.22	163
{Test = WST-1 → High Viability}	0.019	0.57	1.11	45
{Test = Live/Dead → High Viability}	0.020	0.55	1.08	47

Table S2.2. Combined factor associations resulting in high viability (≥ 85%). The associations were listed based on their ranked lift values (above 1).

Material & Shape Association				
Antecedent → Consequent	**Support**	**Confidence**	**Lift**	**Count**
{Material = HAP, Shape = Rod → High Viability}	0.019	1.0	1.95	45
{Material = Chitosan, Shape = Irregular → High Viability}	0.012	1.0	1.95	28
{Material = PLGA, Shape = Sphere → High Viability}	0.018	0.86	1.68	43

{Material = Eudragit RL, Shape = Sphere → High Viability}	0.012	0.78	1.52	28
{Material = Iron oxide, Shape = Sphere → High Viability}	0.052	0.73	1.42	122
{Material = Titanium oxide, Shape = Sphere → High Viability}	0.017	0.71	1.38	41
{Material = Polystyrene, Shape = Sphere → High Viability}	0.036	0.70	1.38	84
{Material = Dendrimer, Shape = Sphere → High Viability}	0.014	0.69	1.34	33
{Material = MWCNT, Shape = Nanotube → High Viability}	0.031	0.65	1.26	73
{Material = Bismuth, Shape = Sphere → High Viability}	0.013	0.55	1.08	31
{Material = Gold, Shape = Sphere → High Viability}	0.054	0.52	1.01	127
Material & Diameter Association				
{Material = HAP, Diameter = 10-25 nm → High Viability}	0.010	1.0	1.95	24
{Material = Iron oxide, Diameter = ≤10 nm → High Viability}	0.017	0.95	1.86	40
{Material = Cerium oxide, Diameter = 10-25 nm → High Viability}	0.012	0.94	1.82	29
{Material = Eudragit RL, Diameter = 100-200 nm → High Viability}	0.012	0.78	1.52	28
{Material = Iron oxide, Diameter = 25-100 nm → High Viability}	0.011	0.75	1.46	27
{Material = Titanium oxide, Diameter = 10-25 nm → High Viability}	0.013	0.75	1.46	30
{Material = Polystyrene, Diameter = 25-100 nm → High Viability}	0.033	0.71	1.38	78
{Material = MWCNT, Diameter = 10-25 nm → High Viability}	0.017	0.71	1.38	41
{Material = Iron oxide,	0.015	0.67	1.31	35

Diameter = 10-25 nm → High Viability}				
{Material = Silver, Diameter = 10-25 nm → High Viability}	0.014	0.61	1.18	34
{Material = Gold, Diameter = ≤10 nm → High Viability}	0.030	0.57	1.11	72
{Material = Bismuth, Diameter = 10-25 nm → High Viability}	0.013	0.55	1.08	31
Material & PDI Association				
{Material = PLGA, PDI = [0, 0.2] → High Viability}	0.010	0.86	1.67	24
{Material = Eudragit RL, PDI = [0, 0.2] → High Viability}	0.012	0.78	1.52	28
{Material = Polystyrene, PDI = [0, 0.2] → High Viability}	0.033	0.75	1.47	77
Material & Test Type Association				
{Material = HAP, Test = CCK-8 → High Viability}	0.019	1.00	1.95	45
{Material = Chitosan, Test = MTT → High Viability}	0.014	0.85	1.66	34
{Material = MWCNT, Test = MTS → High Viability}	0.012	0.80	1.57	29
{Material = Cerium oxide, Test = MTT → High Viability}	0.011	0.77	1.50	27
{Material = Iron oxide, Test = MTT → High Viability}	0.035	0.75	1.47	82
{Material = MWCNT, Test = CCK-8 → High Viability}	0.011	0.74	1.45	26
{Material = Polystyrene, Test = MTT → High Viability}	0.025	0.73	1.42	59
{Material = PLGA, Test = MTT → High Viability}	0.012	0.69	1.35	29
{Material = Gold, Test = NRU → High Viability}	0.012	0.64	1.26	29
{Material = Titanium oxide,	0.011	0.63	1.24	26

Test = MTT → High Viability}				
{Material = Silver, Test = MTS → High Viability}	0.017	0.58	1.13	40
{Material = Silica, Test = CCK-8 → High Viability}	0.014	0.57	1.10	34
Cell Type & Test Type Association				
{Cell Type = MBMC, Test = MTT → High Viability}	0.014	0.97	1.90	34
{Cell Type = SIRC, Test = MTT → High Viability}	0.011	0.83	1.62	25
{Cell Type = SHSY5Y, Test = MTT → High Viability}	0.010	0.75	1.46	24
{Cell Type = HUVEC, Test = CCK-8 → High Viability}	0.029	0.75	1.46	69
{Cell Type = HCMEC, Test = MTT → High Viability}	0.017	0.74	1.44	40
{Cell Type = CCL-110, Test = MTS → High Viability}	0.011	0.57	1.14	47
{Cell Type = A549, Test = MTS → High Viability}	0.011	0.52	1.04	44
Material, Coat & Synthesis Method Association				
{Material = HAP, Coat = None, Synthesis = Precipitation → High Viability}	0.014	1.0	1.95	33
{Material = Chitosan, Coat = None, Synthesis = Ionotropic Gelation → High Viability}	0.014	0.97	1.90	34
{Material = Polystyrene, Coat = COOH, Synthesis = Commercial → High Viability}	0.017	0.79	1.54	41
{Material = Eudragit RL, Coat = None, Synthesis = Emulsion–Solvent Evaporation → High Viability}	0.012	0.78	1.52	28
{Material = Titanium oxide, Coat = None, Synthesis = Commercial → High Viability}	0.023	0.76	1.49	55
{Material = Dendrimer, Coat = None, Synthesis = Commercial → High Viability}	0.010	0.65	1.27	24

{Material = Gold, Coat = None, Synthesis = Chemical Reduction → High Viability}	0.024	0.65	1.26	57
{Material = MWCNT, Coat = None, Synthesis = Commercial → High Viability}	0.014	0.64	1.25	32
Material, Diameter & Surface Charge Association				
{Material = Iron oxide, Diameter ≤ 10 nm, Surface Charge = Negative → High Viability}	0.013	0.94	1.83	31
{Material = Polystyrene, Diameter = (25, 100] nm, Surface Charge = Negative → High Viability}	0.025	0.92	1.80	59
{Material = Eudragit RL, Diameter = (100, 200] nm, Surface Charge = Negative → High Viability}	0.012	0.78	1.52	28
{Material = MWCNT, Diameter = (10, 25] nm, Surface Charge = Negative → High Viability}	0.013	0.64	1.26	31
Material, Diameter & Dose Association				
{Material = Silver, Diameter = (25, 100] nm, Dose < 10 µg/ml → High Viability}	0.012	0.90	1.76	28
{Material = Gold, Diameter ≤ 10 nm, Dose < 10 µg/ml → High Viability}	0.016	0.86	1.68	38
{Material = Polystyrene, Diameter = (25, 100] nm, Dose = [10, 100] µg/ml → High Viability}	0.027	0.70	1.37	64
{Material = Gold, Diameter = (25, 100] nm, Dose < 10 µg/ml → High Viability}	0.011	0.60	1.16	25
{Material = Gold, Diameter = (10, 25] nm, Dose < 10 µg/ml → High Viability}	0.012	0.54	1.05	28
Material, Diameter & Cell Type Association				
{Material = MWCNT, Diameter = (10, 25] nm, Cell Type = HUVEC → High Viability}	0.011	0.75	1.46	27

- The ARM results to investigate the cases which result in low cellular viability are provided in Table S2.3 and Table S2.4.

Table S2.3. Single factor associations resulting in low viability (≤ 50%). The associations were listed based on their ranked lift values (above 1).

Antecedent → Consequent	Support	Confidence	Lift	Count
{Material = Solid-Lipid → Low Viability}	0.014	0.54	2.97	33
{Material = Zinc oxide → Low Viability}	0.020	0.41	2.27	46
{Material = Silver → Low Viability}	0.025	0.27	1.47	59
{Material = Silica → Low Viability}	0.024	0.25	1.36	56
{Material = Gold → Low Viability}	0.033	0.19	1.06	77
{Coat = CTAB → Low Viability}	0.011	0.61	3.36	27
{Coat = Chitosan → Low Viability}	0.014	0.34	1.86	33
{Coat = None → Low Viability}	0.124	0.20	1.09	293
{Synthesis = Sol-Gel Method→ Low Viability}	0.014	0.23	1.24	32
{Synthesis = Commercial → Low Viability}	0.097	0.22	1.19	229
{Shape = Rod → Low Viability}	0.016	0.24	1.32	39
{Shape = Sphere → Low Viability}	0.140	0.19	1.02	330
{Surface Charge = Positive → Low Viability}	0.043	0.24	1.34	102
{Concentration = (200, 1000] μg/ml → Low Viability}	0.037	0.40	2.21	88
{Concentration = (100, 200] μg/ml → Low Viability}	0.020	0.24	1.29	46
{PDI = (0.2, 0.4] → Low Viability}	0.016	0.26	1.40	37
{Cell Type = HaCat → Low Viability}	0.016	0.45	2.48	39
{Cell Type = HepG2 → Low Viability}	0.015	0.19	1.04	36
{Cell Morphology = Keratinocyte → Low Viability}	0.017	0.44	2.41	40
{Cell Morphology = Macrophage → Low Viability}	0.015	0.20	1.11	36
{Cell Morphology = Fibroblast → Low Viability}	0.034	0.19	1.04	80
{Test = Alamar Blue → Low Viability}	0.022	0.36	1.95	52
{Test = MTT → Low Viability}	0.093	0.19	1.05	220

Table S2.4. Combined factor associations resulting in low viability (≤ 50%). The associations were listed based on their ranked lift values (above 1).

Antecedent → Consequent	Support	Confidence	Lift	Count
Material & Shape Association				
{Material = Solid-Lipid, Shape = Sphere → Low Viability}	0.014	0.54	2.97	33
{Material = Zinc oxide, Shape = Sphere → Low Viability}	0.015	0.41	2.26	35
{Material = Silver, Shape = Sphere → Low Viability}	0.023	0.32	1.73	54
{Material = Silica, Shape = Sphere → Low Viability}	0.024	0.25	1.36	56
Material & Diameter Association				
{Material = Zinc oxide, Diameter = (25, 100] nm → Low Viability}	0.014	0.44	2.44	33
{Material = Silver, Diameter = (25, 100] nm → Low Viability}	0.016	0.26	1.43	39
Material & PDI Association				
{Material = Solid-Lipid, PDI = [0, 0.2] → High Viability}	0.014	0.54	2.97	33
Material & Test Association				
{Material = Zinc oxide, Test = MTT → Low Viability}	0.012	0.44	2.40	28
{Material = Gold, Test = MTT → Low Viability}	0.023	0.21	1.17	54
Cell Type & Test Association				
{Cell Type =HepG2, Test = MTT → Low Viability}	0.010	0.21	1.16	24
Material, Coat & Synthesis Method Association				
{Material = Silica, Coat = None, Synthesis = Commercial → Low Viability}	0.014	0.43	2.34	32
{Material = Zinc oxide, Coat = None, Synthesis = Commercial → Low Viability}	0.019	0.42	2.28	44
{Material = Silver, Coat = None, Synthesis = Commercial → Low Viability}	0.014	0.30	1.66	34
Material, Diameter & Surface Charge Association				
{Material = Silver, Diameter = (25, 100] nm, Surface Charge = Negative → Low Viability}	0.015	0.27	1.50	36
Material, Diameter & Dose Association				
{Material = Zinc oxide, Diameter = (25, 100] nm, Dose = [10, 100] µg/ml → Low Viability}	0.013	0.57	3.10	30

Table S2.5. Single factor associations resulting in medium viability (50-85%). The associations were listed based on their ranked lift values (above 1).

Antecedent → Consequent	Support	Confidence	Lift	Count
{Material = Bismuth(III) oxide → Medium Viability}	0.020	0.77	2.51	46
{Material = Fullerene → Medium Viability}	0.014	0.64	2.10	32
{Material = Platinum → Medium Viability}	0.010	0.37	1.21	24
{Material = Gold → Medium Viability}	0.059	0.35	1.14	139
{Material = Silica → Medium Viability}	0.030	0.31	1.03	71
{Coat = Citrate → Medium Viability}	0.020	0.42	1.38	48
{Coat = PEG → Medium Viability}	0.015	0.35	1.15	35
{Coat = None → Medium Viability}	0.191	0.30	1.00	449
{Synthesis = Sol-Gel Method→ Medium Viability}	0.030	0.50	1.65	71
{Synthesis = Green Synthesis → Medium Viability}	0.015	0.49	1.59	36
{Synthesis = Chemical Reduction → Medium Viability}	0.045	0.34	1.13	106
{Synthesis = Chemical Vapor Deposition → Medium Viability}	0.011	0.31	1.01	26
{Shape = Sphere → Medium Viability}	0.240	0.32	1.04	559
{Surface Charge = Negative → Medium Viability}	0.164	0.31	1.02	386
{Concentration = (100, 200] µg/ml → Medium Viability}	0.032	0.38	1.26	75
{Concentration = [10, 100] µg/ml → Medium Viability}	0.160	0.32	1.07	374
{PDI = (0.6, 0.8] → Medium Viability}	0.011	0.48	1.58	27
{Cell Type = HepG2 → Medium Viability}	0.039	0.48	1.58	91
{Cell Type = NR8383 → Medium Viability}	0.010	0.41	1.36	24
{Cell Type = Caco-2 → Medium Viability}	0.011	0.39	1.28	25
{Cell Type = A549 → Medium Viability}	0.033	0.38	1.26	79
{Cell Type = HeLa → Medium Viability}	0.019	0.38	1.25	44
{Cell Morphology = Epithelial → Medium Viability}	0.170	0.34	1.13	398
{Cell Morphology = Fibroblast → Medium Viability}	0.056	0.31	1.01	131
{Test = NRU → Medium Viability}	0.033	0.36	1.17	77
{Test = MTT → Medium Viability}	0.167	0.34	1.12	393
{Test = Live/Dead → Medium Viability}	0.012	0.34	1.12	29
{Test = WST-1 → Medium Viability}	0.011	0.33	1.08	26

Table S2.6. Combined factor associations resulting in medium viability (50-85%). The associations were listed based on their ranked lift values (above 1).

Antecedent → Consequent	Support	Confidence	Lift	Count
Material & Shape Association				
{Material = Bismuth(III) oxide, Shape = Sphere → Medium Viability}	0.020	0.77	2.51	46
{Material = Fullerene, Shape = Sphere → Medium Viability}	0.014	0.64	2.10	32
{Material = Platinum, Shape = Sphere → Medium Viability}	0.010	0.37	1.21	24
{Material = Gold, Shape = Sphere → Medium Viability}	0.036	0.34	1.13	85
{Material = Gold, Shape = Rod → Medium Viability}	0.010	0.34	1.12	24
{Material = Silica, Shape = Sphere → Medium Viability}	0.030	0.31	1.03	71
{Material = Zinc oxide, Shape = Sphere → Medium Viability}	0.011	0.30	1.00	26
Material & Diameter Association				
{Material = Fullerene, Diameter = (25, 100] nm → Medium Viability}	0.011	0.68	2.24	26
{Material = Gold, Diameter = (10, 25] nm → Medium Viability}	0.026	0.61	2.01	62
{Material = Gold, Diameter = (25, 100] nm → Medium Viability}	0.013	0.32	1.06	30
{Material = Silver, Diameter = (25, 100] nm → Medium Viability}	0.020	0.32	1.05	48
Material & Test Association				
{Material = Bismuth(III) oxide, Test = NRU → Medium Viability}	0.011	0.81	2.66	26
{Material = Silica,	0.020	0.43	1.41	46

Test = MTT → Medium Viability}				
{Material = Gold, Test = MTT → Medium Viability}	0.042	0.39	1.28	99
{Material = Silver, Test = MTS → Medium Viability}	0.011	0.36	1.19	25
Cell Type & Test Association				
{Cell Type =HepG2, Test = MTT → Medium Viability}	0.028	0.57	1.88	65
{Cell Type =A549, Test = MTT → Medium Viability}	0.020	0.55	1.79	47
Material, Coat & Synthesis Method Association				
{Material = Bismuth(III) oxide, Coat = None, Synthesis = Commercial → Medium Viability}	0.020	0.77	2.51	46
{Material = Silica, Coat = None, Synthesis = Sol-Gel Method → Medium Viability}	0.020	0.55	1.81	48
{Material = Gold, Coat = Citrate, Synthesis = Chemical Reduction → Medium Viability}	0.012	0.49	1.61	28
{Material = Silver, Coat = None, Synthesis = Commercial → Medium Viability}	0.015	0.31	1.02	35
Material, Diameter & Surface Charge Association				
{Material = Fullerene, Diameter = (25, 100] nm, Surface Charge = Negative → Medium Viability}	0.011	0.68	2.24	26
Material, Diameter & Dose Association				
{Material = Silver, Diameter = (25, 100] nm, Dose = [10, 100] μg/ml → Medium Viability}	0.018	0.47	1.55	42
{Material = Gold, Diameter = (10, 25] nm, Dose < 10 μg/ml → Medium Viability}	0.010	0.46	1.51	24

ABBREVIATIONS

A549, human lung alveolar epithelial cells; ARM, association rule mining; Caco-2, human colon adenocarcinoma cell line; CCK-8, cell counting kit - 8; CCL-110, human skin fibroblast cell line; CTAB, cetyltrimethylammonium bromide; HaCat, human epidermal keratinocyte cell line; HAP, hydroxyapatite; HCMEC, human cardiac microvascular endothelial cells; HeLa, human cervix epithelial cell line; HepG2, human liver cancer cell line; HUVEC, human umbilical vein endothelial cells; J774A.1, mouse ascites reticulum cell line; L929, murine fibroblast cell line; LDH, lactate dehydrogenase; MBMC, mouse bone-marrow derived stem cells; MG-63, human osteosarcoma cell line; MTS, 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium; MTT, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; MWCNT, multi-walled carbon nanotube; NP, nanoparticle; NR8383, rat alveolar macrophage cell line; NRU, neutral red uptake; PC12, rat pheochromocytoma cell line; PDI, polydispersity index; PEG, polyethylene glycol; PLGA, poly (lactic-co-glycolic acid); RAW264.7, murine macrophage cell line; SHSY5Y, human neuroblastoma cell line; SIRC, statens seruminstitut rabbit cornea cell line; THP-1, human monocytic cell line; WST-1, water soluble tetrazolium; XTT, 2,3-bis-(2-methoxy-4-nitro-5-sulfophenyl)-2H-tetrazolium-5-carboxanilide.

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