

Each ODT sample = 1
dried tablet from
0.5ml dose wt.
dissolved in 5 ml
water (diluted x10)

Each ODT sample = 1
dried tablet from 0.5ml
dose wt dissolved in 5 ml
water (diluted x10)

BCS class	API	API Conc (in test sample) mg/ml Preform/ODT	Permeation agent (PA)	PA Conc (in CMC) Preform/ODT	PA Conc (in Molar Ratio API: PA) Preform/ODT	PA Conc (in test sample) mg/ml Preform/ODT	PA Conc (in binary mix/ form'tn) % Preform/ODT	Preformulation Permeability	ODT Permeability
2sub gp1	Carvedilol	1.74 / ND	PF127	2CMC / ND	-	1 / ND	0.1 / ND	No significant change	ND
2sub gp1	Carvedilol	1.74 / ND	PF127 + Citric acid	2CMC / ND	-	1 / ND	0.1 / ND	Enhance	ND
2sub gp2	Piroxicam	0.7 / ND	PF127	0.5 CMC / ND	-	0.25 / ND	0.025 / ND	Enhance	ND
2sub gp2	Piroxicam	0.7 / ND	PF127	1 CMC / ND	-	0.5 / ND	0.05 / ND	Enhance	ND
2sub gp2	Piroxicam	0.7 / 4	PF127	2 CMC / 2CMC	-	1 / 0.1	0.1 / 0.1	Enhance	Enhance
2sub gp2	Piroxicam	ND / 4	PF127	ND / 5 CMC	-	ND / 0.25	ND / 0.25	ND	Not tested
2sub gp2	Piroxicam	ND / 4	PF127	ND / 10CMC	-	ND / 0.5	ND / 0.5	ND	Not tested
2sub gp2	Piroxicam	ND / 4	PF127	ND / 20 CMC	-	ND / 1	ND / 1	ND	Enhance
2sub gp2	Piroxicam	ND / 4	PF127	ND / 30 CMC	-	ND / 1.5	ND / 1.5	ND	Enhance
3subgp 1	Famotidine	1.4/ ND	PF127	2CMC / ND	-	1 / ND	0.1 / ND	No significant change	ND
3subgp2	Atenolol	1.74 / ND	PF127	2CMC / ND	-	1 / ND	0.1 / ND	No significant change	ND

FIG. 1A

BCS class	API	API Conc (in test sample) mg/ml Preform/ODT	Permeation agent (PA)	PA Conc (in CMC) Preform/ODT	PA Conc (in Molar Ratio API: PA) Preform/ODT	PA Conc (in test sample) mg/ml Preform/ODT	PA Conc (in binary mix/ form'ltn) % Preform/ODT	Preformulation Permeability	ODT Permeability
2sub gp1	Carvedilol	ND	PL44	ND	ND	ND	ND	ND	ND
2sub gp2	Piroxicam	0.7 / ND	PL44	2CMC / ND	3.5:1 / ND	15.84 / ND	1.54 / ND	No significant change → Enhance	ND
3subgp 1	Famotidine	ND	PL44	ND	ND	ND	ND	ND	ND
3subgp2	Atenolol	ND	PL44	ND	ND	ND	ND	ND	ND
2subgp1	Piroxicam	0.7 / ND	Tween 21	-	1:1 / ND	1.19 / ND	0.119 / ND	Enhance	ND
2subgp2	Carvedilol	1.74 / ND	Tween 21	-	1:1 / ND	2.41 / ND	0.241 / ND	No significant change → Enhance	ND
3subgp1	Famotidine	1.4 / ND	Tween 21	-	1:1 / ND	2.34 / ND	0.234 / ND	No significant change	ND
3subgp2	Atenolol	1.74 / ND	Tween 21	-	1:1 / ND	3.68 / ND	0.368 / ND	No significant change	ND
2subgp1	Carvedilol	1.74 / ND	SLS	-	1:1 / ND	1.21 / ND	0.12 / ND	No significant change → Enhance	ND
2subgp 2	Piroxicam	ND / 4	SLS	-	ND / 5:1	ND / 0.69	ND / 0.69	ND	Enhance
2 subgp2	Piroxicam	ND / 4	SLS	-	ND / 4:1	ND / 0.88	ND / 0.88	ND	Not tested
2 subgp2	Piroxicam	ND / 4	SLS	-	ND / 3:1	ND / 1.17	ND / 1.17	ND	Not tested
2 subgp2	Piroxicam	ND / 4	SLS	-	ND / 2:1	ND / 1.73	ND / 1.73	ND	Not tested

FIG. 1A
CONTINUED

BCS class	API	API Conc (in test sample) mg/ml Preform/ODT	Permeation agent (PA)	PA Conc (in CMC) Preform/ODT	PA Conc (in Molar Ratio API: PA) Preform/ODT	PA Conc (in test sample) mg/ml Preform/ODT	PA Conc (in binary mix/ form'lt'n) % Preform/ODT	Preformulation Permeability	ODT Permeability
2 subgp2	Piroxicam	0.7 / 4	SLS	-	ND / 1:1	0.61 / 3.49	0.06 / 3.49	No significant change → Enhance	Enhance
3 subgp1	Famotidine	ND	SLS	-	ND	ND	ND	ND	ND
3 subgp2	Atenolol	1.74 / ND	SLS	-	1:1 / ND	1.88 / ND	0.188 / ND	No significant change	ND
2 subgp1	Carvedilol	1.74 / ND	DDM	-	1:1 / ND	2.07 / ND	0.207 / ND	No significant change	ND
2 subgp2	Piroxicam	0.7 / ND	DDM	-	1:1 / ND	1.015 / ND	0.1 / ND	No significant change → Enhance	ND
3 subgp 1	Famotidine	1.4 / ND	DDM	-	1:1 / ND	2 / ND	0.2 / ND	Enhance → No significant change	ND
3 subgp 2	Atenolol	1.74 / ND	DDM	-	1:1 / ND	3.15 / ND	0.315 / ND	No significant change	ND
2 subgp 1	Carvedilol	1.74 / ND	Span 80	-	1:1 / ND	1.86 / ND	0.186 / ND	Inhibit	ND
2 subgp 2	Piroxicam	0.7 / ND	Span 80	-	1:1 / ND	0.91 / ND	0.09 / ND	Inhibit	ND
3 subgp 1	Famotidine	1.4 / ND	Span 80	-	1:1 / ND	1.82 / ND	0.182 / ND	Enhance	ND
3 subgp2	Atenolol	1.74 / ND	Span 80	-	1:1 / ND	2.8 / ND	0.28 / ND	No significant change	ND

FIG. 1A
CONTINUED

Each ODT sample =
1 dried tablet from
0.5ml dose wt
Data dissolved in 5 ml
water (diluted x10)

Each ODT sample = 1
dried tablet from 0.5ml
dose wt dissolved in 5 ml
water (diluted x10)

BCS class	API	API Conc (in test sample) mg/ml Preform/ODT	Permeation agent (PA)	PA Conc (in CMC) Preform/ODT	PA Conc (in Molar Ratio API: PA) Preform/ODT	PA Conc (in test sample) mg/ml Preform/ODT	PA Conc (in binary mix/ form'tn) % Preform/ODT	Preformulation Permeability	ODT Permeability
2 subgp 1	Carvedilol	1.74 / ND	Sodium cholate	2 CMC / ND	1: 7.4 / ND	13.46 / ND	1.36 / ND	No significant change ➔ Enhance	ND
2 subgp 1	Carvedilol	1.74 / ND	Sodium cholate + citric acid	2 CMC / ND	1: 7.4 / ND	13.46 / ND	1.36 / ND	No significant change ➔ Enhance	ND
2 subgp 2	Piroxicam	0.7 / 4	Sodium cholate	0.5 CMC / 0.5 CMC	1: 3.7 / 15:1	3.4 / 0.34	0.34 / 0.34	Slight	Enhance
2 subgp 2	Piroxicam	0.7 / 4	Sodium cholate	1 CMC / 1 CMC	1: 7.5 / 7.6: 1	6.8 / 0.68	0.68 / 0.68	Enhance	Not tested
2 subgp 2	Piroxicam	0.7 / 4	Sodium cholate	2 CMC / 2 CMC	1: 14.9 / 3.8: 1	13.6 / 1.36	1.36 / 1.36	Enhance	Not tested
2 subgp 2	Piroxicam	0.7 / ND	Sodium cholate + citric acid	2 CMC / ND	1: 14.9 / ND	13.6 / ND	1.36 / ND	Slight	ND
2 subgp 2	Piroxicam	ND / 4	Sodium cholate	ND / 4 CMC	ND / 1.9:1	ND / 2.72	ND / 2.72	ND	Enhance
3 subgp 1	Famotidine	1.4 / ND	Sodium cholate	2 CMC / ND	1: 7.6 / ND	13.46 / ND	1.36 / ND	Enhance	ND
3 subgp 2	Atenolol	1.74 / ND	Sodium cholate	2 CMC / ND	1: 4.8 / ND	13.46 / ND	1.36 / ND	No significant change	ND

FIG. 1B

Each ODT sample =
1 dried tablet from
0.5ml dose wt
No Data dissolved in 5 ml
water (diluted x10)

Each ODT sample = 1
dried tablet from 0.5ml
dose wt dissolved in 5 ml
water (diluted x10)

BCS class	API	API Conc (in test sample) mg/ml Preform/ODT	Permeation agent (PA)	PA Conc (in CMC) Preform/ODT	PA Conc (in Molar Ratio API: PA) Preform/ODT	PA Conc (in test sample) mg/ml Preform/ODT	PA Conc (in binary mix/ form'ltn) % Preform/ODT	Preformulation Permeability	ODT Permeability
2 subgp 1	Carvedilol	1.74 / ND	Capric acid	-	1:2 / ND	1.5 / ND	0.15 / ND	No significant change → Enhance	ND
2 subgp 2	Piroxicam	0.7 / ND	Capric acid	-	1:1 / ND	0.364 / ND	0.036 / ND	Inhibit	ND
3 subgp 1	Famotidine	ND	Capric acid	ND	ND	ND	ND	ND	ND
3 subgp 2	Atenolol	ND	Capric acid	ND	ND	ND	ND	ND	ND

FIG. 1C

Each ODT sample =
1 dried tablet from
0.5ml dose wt
dissolved in 5 ml
water (diluted x10)

Each ODT sample = 1
dried tablet from 0.5ml
dose wt dissolved in 5 ml
water (diluted x10)

ND=
No Data

BCS class	API	API Conc (in test sample) mg/ml Preform/ODT	Permeation agent (PA)	PA Conc (in CMC) Preform/ODT	PA Conc (in Molar Ratio API: PA) Preform/ODT	PA Conc (in test sample) mg/ml Preform/ODT	PA Conc (in binary mix/form/ltm) % Preform/ODT	Preformulation Permeability	ODT Permeability
2 subgp 1	Carvedilol	1.74 / ND	Citric acid	-	16.5:1 / ND	0.05 / ND	0.005 / ND	Enhance	ND
2 subgp 1	Carvedilol	1.74 / ND	Citric acid	-	1.65:1 / ND	0.5 / ND	0.05 / ND	No significant change → Enhance	ND
2 subgp 2	Piroxicam	ND	Citric acid	ND	ND	ND	ND	ND	ND
3 subgp 1	Famotidine	ND	Citric acid	ND	ND	ND	ND	ND	ND
3 subgp 2	Atenolol	1.74 / ND	Citric acid	-	3.4:1 / ND	0.37 / ND	0.037 / ND	Inhibit	ND
3 subgp 2	Atenolol	1.74 / ND	Citric acid	-	2.5:1 / ND	0.50 / ND	0.050 / ND	Inhibit	ND
3 subgp 2	Atenolol	1.74 / ND	Citric acid	-	1.25:1 / ND	1.0 / ND	0.10 / ND	Inhibit	ND

FIG. 1D

Each ODT sample =
1 dried tablet from
0.5ml dose wt
No Data
dissolved in 5 ml
water (diluted x10)

Each ODT sample = 1
dried tablet from 0.5ml
dose wt dissolved in 5 ml
water (diluted x10)

BCS class	API	API Conc (in test sample) mg/ml Preform/ODT	Permeation agent (PA)	PA Conc (in CMC) Preform/ ODT	PA Conc (in Molar Ratio API: PA) Preform/ODT	PA Conc (in test sample) mg/ml Preform/ODT	PA Conc (in binary mix/ form'ltn) % Preform/ODT	Preformulation Permeability	ODT Permeability
2 subgp 1	Carvedilol	1.74 / ND	Aspartic acid	-	1:1 / ND	0.58 / ND	0.058 / ND	No significant change Enhance	ND
2 subgp 1	Carvedilol	1.74 / ND	Aspartic acid + NaOH	-	1:3 / ND	1.74 / ND	0.174 / ND	No significant change Enhance	ND
2 subgp 1	Carvedilol	1.74 / ND	Aspartic acid + NaOH	-	1:6 / ND	3.48 / ND	0.348 / ND	No significant change Enhance	ND
2 subgp 1	Carvedilol	1.74 / ND	Alanine + HCL	-	1:1 / ND	0.4 / ND	0.04 / ND	No significant change	ND
2 subgp 2	Piroxicam	0.7 / ND	Arginine + HCL	-	1:1 / ND	0.4 / ND	0.04 / ND	Enhance	ND
2 subgp 2	Piroxicam	0.7 / ND	Arginine + HCL	-	1:3 / ND	1.12 / ND	0.125 / ND	Enhance	ND
2 subgp 2	Piroxicam	0.7 / ND	Arginine + HCL	-	1:6 / ND	2.2 / ND	0.22 / ND	No significant change	ND
2 subgp 2	Piroxicam	0.7 / ND	Lysine + HCL	-	1:3 / ND	0.93 / ND	0.093 / ND	No significant change	ND
2 subgp 2	Piroxicam	0.7 / ND	Lysine + HCL	-	1:6 / ND	1.85 / ND	0.185 / ND	No significant change	ND

FIG. 1E

BCS class	API	API Conc'n (in test sample) mg/ml Preform/ODT	Permeation agent (PA)	PA Conc'n (in CMC) Preform/ ODT	PA Conc (in Molar Ratio API: PA) Preform/ODT	PA Conc'n (in test sample) mg/ml Preform/ODT	PA Conc'n (in binary mix/ form'ltm) % Preform/ODT	Preformulation Permeability	ODT Permeability
3 subgp 1	Famotidine	1.4 / ND	Glycine	-	1:1 / ND	0.32 / ND	0.032 / ND	Enhance	ND
3 subgp 1	Famotidine	1.4 / ND	Glycine + HCL	-	1:3 / ND	0.94 / ND	0.094 / ND	Enhance → No significant change	ND
3 subgp 1	Famotidine	1.4 / ND	Glycine + NaOH	-	1:3 / ND	0.94 / ND	0.094 / ND	Enhance	ND
3 subgp 1	Famotidine	1.4 / ND	Aspartic acid	-	1:1 / ND	0.56 / ND	0.056 / ND	No significant change	ND
3 subgp 1	Famotidine	1.4 / ND	Aspartic acid + NaOH	-	1:1 / ND	0.56 / ND	0.056 / ND	Enhance → No significant change	ND
3 subgp 1	Famotidine	1.4 / ND	Aspartic acid + NaOH	-	1:3 / ND	1.65 / ND	0.165 / ND	No significant change	ND
3 subgp 1	Famotidine	1.4 / ND	Benzoic acid + NaOH	-	1:1 / ND	0.5 / ND	0.05 / ND	No significant change	ND
3 subgp 2	Atenolol	1.74 / ND	Aspartic acid	-	3: 1/ ND	0.58 / ND	0.058 / ND	No significant change	ND
3 subgp 2	Atenolol	1.74 / ND	Aspartic acid	-	1:1 / ND	0.87 / ND	0.087 / ND	Enhance	ND
3 subgp 2	Atenolol	1.74 / ND	Aspartic acid+ NaOH	-	1:3 / ND	2.61 / ND	0.261 / ND	Enhance	ND
3 subgp 2	Atenolol	1.74 / ND	Benzoic+NaOH	-	1:1 / ND	0.78 / ND	0.078 / ND	Enhance	ND

FIG. 1E
CONTINUED

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Preformulation: API: PA Binary Mix					
API	PA category	Permeation agent (PA)	API concentration in test sample	PA concentration in test sample	Permeability test relative to control
Atenolol	Surfactant	PF127	1.74 mg/ml	2CMC (1 mg/ml)	No effect
Atenolol	Surfactant	SLS	1.74 mg/ml	1:1 molar ratio to ATL (1.88 mg/ml)	No effect
Atenolol	Surfactant	Tween 21	1.74 mg/ml	1:1 molar ratio to ATL (3.68 mg/ml)	No effect
Atenolol	Surfactant	DDM	1.74 mg/ml	1:1 molar ratio to ATL (3.15 mg/ml)	No effect
Atenolol	Surfactant	Span 80	1.74 mg/ml	1:1 molar ratio to ATL (2.8 mg/ml)	No effect
Atenolol	Bile Salt	Sodium Cholate	1.74 mg/ml	2CMC (13.46 mg/ml)	No effect
Atenolol	Fatty Acid				
Atenolol	pH modifier	Citric acid	1.74 mg/ml	0.37 mg/ml	Inhibit
Atenolol	pH modifier	Citric acid	1.74 mg/ml	0.5 mg/ml	Inhibit
Atenolol	pH modifier	Citric acid	1.74 mg/ml	1 mg/ml	Inhibit
Atenolol	Counterion	Aspartic acid	1.74 mg/ml	3:1 molar ratio ATL: Aspartic acid (0.58 mg/ml)	No change
Atenolol	Counterion	Aspartic acid	1.74 mg/ml	1:1 molar ratio ATL: Aspartic acid (0.87 mg/ml)	Enhance
Atenolol	Counterion	Aspartic acid	1.74 mg/ml	1:3 molar ratio ATL: Aspartic acid (2.61 mg/ml) adjusted with 0.1NaOH	Enhance
Atenolol	Counterion	Benzoic acid	1.74 mg/ml	1:1 molar ratio ATL: Benzoic acid (0.78 mg/ml) adjusted with 0.1NaOH	Enhance

FIG. 2A

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			Preformulation: API: PA Binary Mix		
API	PA category	Permeation agent (PA)	API concentration in test sample	PA concentration in test sample	Permeability test relative to control
Carvedilol	Surfactant	PF127	1.74 mg/ml	2CMC (1 mg/ml)	No effect
Carvedilol	Surfactant	PF127 (+ citric acid as pH modifier)	1.74 mg/ml	2CMC (1 mg/ml), plus 0.5 mg/ml citric acid	Enhance
Carvedilol	Surfactant	SLS	1.74 mg/ml	1:1 molar ratio CAV: SLS (1.21 mg/ml)	Enhance
Carvedilol	Surfactant	DDM	1.74 mg/ml	1:1 molar ratio CAV:DDM ratio (2.07 mg/ml)	No change
Carvedilol	Surfactant	Tween 21	1.74 mg/ml	1:1 molar ratio CAV:TW21 (2.41 mg/ml)	Enhance
Carvedilol	Surfactant	Span 80	1.74 mg/ml	1:1 molar ratio CAV:S80 (1.86 mg/ml)	Inhibit
Carvedilol	Bile Salt	Sodium Cholate	1.74 mg/ml	2CMC (13.46 mg/ml)	Enhance
Carvedilol	Bile Salt	Sodium Cholate (+ citric acid as pH modifier)	1.74 mg/ml	2CMC (13.46 mg/ml)	Enhance
Carvedilol	Fatty Acid	Capric acid	1.74 mg/ml	1:2 molar ratio CAV:CA (1.5mg/ml)	Enhance
Carvedilol	pH modifier	Citric acid	1.74 mg/ml	0.05 mg/ml	Enhance
Carvedilol	pH modifier	Citric acid	1.74 mg/ml	0.5 mg/ml	Enhance
Carvedilol	Counterion	Aspartic acid	1.74 mg/ml	1:1 molar ratio CAV: Aspartic acid (0.58 mg/ml)	Enhance
Carvedilol	Counterion	Aspartic acid (+0.1M NaOH as pH modifier)	1.74 mg/ml	1:3 molar ratio CAV: Aspartic acid (1.74 mg/ml) adjusted with 0.1M NaOH	Enhance

FIG. 2B

			Preformulation: API: PA Binary Mix		
API	PA category	Permeation agent (PA)	API concentration in test sample	PA concentration in test sample	Permeability test relative to control
Carvedilol	Counterion	Aspartic acid (+0.1M NaOH as pH modifier)	1.74 mg/ml	1:6 molar ratio CAV: Aspartic acid (3.48 mg/ml) adjusted with 0.1M NaOH	Enhance
Carvedilol	Counterion	Alanine (+0.1M HCL as pH modifier)	1.74 mg/ml	1:1 molar ratio CAV: Alanine acid (0.4 mg/ml)	Enhance

FIG. 2B
CONTINUED

			Preformulation: API: PA Binary Mix		
API	PA category	Permeation agent (PA)	API concentration in test sample	PA concentration in test sample	Permeability test relative to control
Famotidine	Surfactant	PF127	1.4 mg/ml	2CMC (1 mg/ml)	No effect
Famotidine	Surfactant	Tween 21	1.4 mg/ml	1:1 molar ratio FAM:TW21 (2.34 mg/ml)	No effect
Famotidine	Surfactant	DDM	1.4 mg/ml	1:1 molar ratio FAM:DDM (2 mg/ml)	Enhance
Famotidine	Surfactant	Span 80	1.4 mg/ml	1:1 molar ratio FAM:S80 (1.82 mg/ml)	Enhance
Famotidine	Bile Salt	Sodium Cholate	1.4 mg/ml	2CMC (13.46 mg/ml)	Enhance
Famotidine	Fatty Acid	-	-	-	-
Famotidine	pH modifier	-	-	-	-
Famotidine	Counterion	Glycine	1.4 mg/ml	1:3 molar ratio FAM: Glycine (0.94 mg/ml) adjusted with 0.1M HCl	No effect
Famotidine	Counterion	Glycine	1.4 mg/ml	1:3 molar ratio FAM: Glycine (0.94 mg/ml) adjusted with 0.1M NaOH	Enhance
Famotidine	Counterion	Glycine	1.4 mg/ml	1:1 molar ratio FAM: Glycine (0.32 mg/ml)	Enhance
Famotidine	Counterion	Aspartic acid	1.4 mg/ml	1:1 molar ratio FAM: Aspartic acid (0.56 mg/ml)	Inhibit

FIG. 2C

			Preformulation: API: PA Binary Mix		
API	PA category	Permeation agent (PA)	API concentration in test sample	PA concentration in test sample	Permeability test relative to control
Famotidine	Counterion	Aspartic acid	1.4 mg/ml	1:1 molar ratio FAM: Aspartic acid (0.56 mg/ml) adjusted with 0.1NaOH	Enhance
Famotidine	Counterion	Aspartic acid	1.4 mg/ml	1:3 molar ratio FAM: Aspartic acid (1.65 mg/ml) adjusted with 0.1NaOH	Inhibit
Famotidine	Counterion	Benzoic acid	1.4 mg/ml	1:1 molar ratio FAM: Benzoic acid (0.5 mg/ml) adjusted with 0.1NaOH	Inhibit

FIG. 2C
CONTINUED

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Col. 1

Col. 2

Col. 3

Col. 4

Col. 5

Col. 6

Preformulation: API: PA Binary Mix						
	API	PA category	Permeation agent (PA)	API concentration in test sample	PA concentration in test sample	Permeability test relative to control
Row 1	Piroxicam	Surfactant	PF127	0.7 mg/ml	0.5CMC (0.25 mg/ml)	Enhance
Row 2	Piroxicam	Surfactant	PF127	0.7 mg/ml	1CMC (0.5 mg/ml)	Enhance
Row 3	Piroxicam	Surfactant	PF127	0.7 mg/ml	2 CMC (1mg/ml)	Enhance
Row 4	Piroxicam	Surfactant	PF127	ND	ND	ND
Row 5	Piroxicam	Surfactant	PF127	ND	ND	ND
Row 6	Piroxicam	Surfactant	PF127	ND	ND	ND
Row 7	Piroxicam	Surfactant	PF127	ND	ND	ND
Row 8	Piroxicam	Surfactant	PL44	0.7 mg/ml	2CMC (15.84 mg/ml)	Enhance
Row 9	Piroxicam	Surfactant	Tween 21	0.7 mg/ml	1:1 molar ratio PXM:TW21 (1.19 mg/ml)	Enhance
Row 10	Piroxicam	Surfactant	Span 80	0.7 mg/ml	1:1 molar ratio PXM:S80 (0.91 mg/ml)	Inhibit
Row 11	Piroxicam	Surfactant	Blend – 5:1 ratio of Tween 21 to Span 80	0.7 mg/ml	1:1 molar ratio PXM: TW21-S80 blend (0.95 mg/ml Tween 21, 0.19 mg/ml Span 80)	Enhance

FIG. 2D

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	Col. 7	Col. 8	Col. 9	Col.10	Col. 11	Col. 12
	ODT (orally disintegrating tablet)					
	ODT Composition Pre Freeze Drying (Aqueous dispersion) Base matrix: 5% gelatin, 4 % mannitol	ODT Composition Post Freeze Drying	API concentration in test sample (reconstituted ODT in 5ml)	PA concentration in test sample (reconstituted ODT in 5ml)	Base matrix concentration in test sample (reconstituted ODT in 5ml)	Permeability test relative to control
Row 1	ND	ND	ND	ND	ND	ND
Row 2	ND	ND	ND	ND	ND	ND
Row 3	PA at 2CMC in aq dispersion (API - 4% w/w, PA - 0.1 % w/w, base matrix - 9% w/w)	API - 30.5% w/w PA - 0.8 % w/w Base matrix - 68.7% w/w	4mg/ml	0.1mg/ml	9mg/ml	Enhance
Row 4	PA at 5CMC in aq dispersion (API - 4% w/w, PA - 0.25 % w/w, base matrix - 9% w/w)	API - 30.2% w/w PA - 1.9 % w/w Base matrix - 67.9% w/w	4mg/ml	0.25mg/ml	9mg/ml	Not tested
Row 5	PA at 10CMC in aq dispersion (API - 4% w/w, PA - 0.5 % w/w (10CMC in aq dispersion), base matrix - 9% w/w)	API - 29.6% w/w PA - 3.7 % w/w Base matrix - 66.7% w/w	4mg/ml	0.5mg/ml	9mg/ml	Not tested
Row 6	PA at 20CMC in aq dispersion (API - 4% w/w, PA - 1.0 % w/w (20CMC in aq dispersion), base matrix - 9% w/w)	API - 28.6% w/w PA - 7.1 % w/w Base matrix - 64.3% w/w	4mg/ml	1.0mg/ml	9mg/ml	Enhance
Row 7	PA at 30CMC in aq dispersion (API - 4% w/w, PA - 1.5% w/w, base matrix - 9% w/w)	API - 27.6% w/w PA - 10.3 % w/w Base matrix - 62.1% w/w	4mg/ml	1.5mg/ml	9mg/ml	Enhance
Row 8	ND	ND	ND	ND	ND	ND
Row 9	ND	ND	ND	ND	ND	ND
Row 10	ND	ND	ND	ND	ND	ND
Row 11	ND	ND	ND	ND	ND	ND

FIG. 2D
CONTINUED

Col. 1	Col. 2	Col. 3	Col. 4	Col. 5	Col. 6	
Preformulation: API: PA Binary Mix						
	API	PA category	Permeation agent (PA)	API concentration in test sample	PA concentration in test sample	Permeability test relative to control
Row 12	Piroxicam	Surfactant	SLS	ND	ND	ND
Row 13	Piroxicam	Surfactant	SLS	ND	ND	ND
Row 14	Piroxicam	Surfactant	SLS	ND	ND	ND
Row 15	Piroxicam	Surfactant	SLS	ND	ND	ND
Row 16	Piroxicam	Surfactant	SLS	0.7 mg/ml	1:1 molar ratio PXM:SLS (0.609 mg/ml)	Enhance
Row 17	Piroxicam	Surfactant	DDM	0.7 mg/ml	1:1 molar ratio PXM:DDM (1.015 mg/ml)	Enhance
Row 18	Piroxicam	Bile Salt	Sodium Cholate	0.7mg/ml	0.5 CMC (3.4mg/ml)	Slight
Row 19	Piroxicam	Bile Salt	Sodium Cholate	0.7mg/ml	1 CMC (6.8mg/ml)	Enhance

FIG. 2D
CONTINUED

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	Col. 7	Col. 8	Col. 9	Col.10	Col. 11	Col. 12
	ODT (orally disintegrating tablet)					
	ODT Composition Pre Freeze Drying (Aqueous dispersion) Base matrix: 5% gelatin, 4 % mannitol	ODT Composition Post Freeze Drying	API concentration in test sample (reconstituted ODT in 5ml)	PA concentration in test sample (reconstituted ODT in 5ml)	Base matrix concentration in test sample (reconstituted ODT in 5ml)	Permeability test relative to control
Row 12	5:1 molar ratio PXM:SLS in aq phase (API - 4% w/w, PA - 0.69% w/w, base matrix - 9% w/w)	API - 29.2% w/w PA - 5.1 % w/w Base matrix - 65.7% w/w	4mg/ml	0.69mg/ml	9mg/ml	Enhance
Row 13	4:1 molar ratio PXM:SLS in aq phase (API - 4% w/w, PA - 0.88% w/w, base matrix - 9% w/w)	API - 28.8% w/w PA - 6.3 % w/w Base matrix - 64.9% w/w	4mg/ml	0.88mg/ml	9mg/ml	Not tested
Row 14	3:1 molar ratio PXM:SLS in aq phase (API - 4% w/w, PA - 1.17% w/w, base matrix - 9% w/w)	API - 28.2% w/w PA - 8.3 % w/w Base matrix - 63.5% w/w	4mg/ml	1.17mg/ml	9mg/ml	Not tested
Row 15	2:1 molar ratio PXM:SLS in aq phase (API - 4% w/w, PA - 1.73% w/w, base matrix - 9% w/w)	API - 27.2% w/w PA - 11.7 % w/w Base matrix - 61.1% w/w	4mg/ml	1.73mg/ml	9mg/ml	Not tested
Row 16	1:1 molar ratio PXM:SLS in aq phase (API - 4% w/w, PA - 3.49% w/w, base matrix - 9% w/w)	API - 24.3% w/w PA - 21.2 % w/w Base matrix - 54.5% w/w	4mg/ml	3.49mg/ml	9mg/ml	Enhance
Row 17	ND	ND	ND	ND	ND	ND
Row 18	PA at 0.5MC in aq dispersion (API - 4% w/w, PA -0.34 % w/w, base matrix - 9% w/w)	API - 30% w/w PA - 2.5% w/w Base matrix - 67.5% w/w	4mg/ml	0.34mg/ml	9mg/ml	Enhance
Row 19	PA at 1CMC in aq dispersion (API - 4% w/w, PA -0.68 % w/w, base matrix - 9% w/w)	API - 29.2% w/w PA - 4.97% w/w Base matrix - 65.83% w/w	4mg/ml	0.68 mg/ml	9mg/ml	Not tested

FIG. 2D
CONTINUED

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Col. 1	Col. 2	Col. 3	Col. 4	Col. 5	Col. 6	
Preformulation: API: PA Binary Mix						
	API	PA category	Permeation agent (PA)	API concentration in test sample	PA concentration in test sample	Permeability test relative to control
Row 20	Piroxicam	Bile Salt	Sodium Cholate	0.7mg/ml	2CMC (13.6mg/ml)	Enhance
Row 21	Piroxicam	Bile Salt	Sodium Cholate (+ citric acid as pH modifier)	0.7 mg/ml	2CMC (13.6 mg/ml) + Citric acid (2mg/ml)	Slight
Row 22	Piroxicam	Bile Salt	Sodium Cholate	ND	ND	ND
Row 23	Piroxicam	Fatty Acid	Capric acid	0.7 mg/ml	1:1 molar ratio PXM:CA (0.364mg/ml)	Inhibit
Row 24	Piroxicam	pH modifier	ND	ND	ND	ND
Row 25	Piroxicam	Counterion	Arginine	0.7 mg/ml	1: 1 molar ratio PXM: Arginine (0.4 mg/ml) adjusted with 0.1MHCl	Enhance
Row 26	Piroxicam	Counterion	Arginine	0.7 mg/ml	1: 3 molar ratio PXM: Arginine (1.12 mg/ml) adjusted with 0.1MHCl	Enhance
Row 27	Piroxicam	Counterion	Arginine	0.7 mg/ml	1: 6 molar ratio PXM: Arginine (2.20 mg/ml) adjusted with 0.1MHCl	Enhance
Row 28	Piroxicam	Counterion	Lysine	0.7 mg/ml	1: 3 molar ratio PXM: Lysine (0.93 mg/ml) adjusted with 0.1MHCl	No change
Row 29	Piroxicam	Counterion	Lysine	0.7 mg/ml	1: 6 molar ratio PXM: Lysine (1.85 mg/ml) adjusted with 0.1MHCl	No change

FIG. 2D
CONTINUED

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	Col. 7	Col. 8	Col. 9	Col.10	Col. 11	Col. 12
	ODT (orally disintegrating tablet)					
	ODT Composition Pre Freeze Drying (Aqueous dispersion) Base matrix: 5% gelatin, 4 % mannitol	ODT Composition Post Freeze Drying	API concentration in test sample (reconstituted ODT in 5ml)	PA concentration in test sample (reconstituted ODT in 5ml)	Base matrix concentration in test sample (reconstituted ODT in 5ml)	Permeability test relative to control
Row 20	PA at 2CMC in aq dispersion (API - 4% w/w, PA -1.36 % w/w, base matrix - 9% w/w)	API - 27.9% w/w PA - 9.5% w/w Base matrix - 62.6% w/w	4mg/ml	1.36mg/ml	9mg/ml	Not tested
Row 21	ND	ND	ND	ND	ND	ND
Row 22	PA at 4CMC in aq dispersion (API - 4% w/w, PA -2.72 % w/w, base matrix - 9% w/w)	API - 25.4% w/w PA - 17.3% w/w Base matrix - 57.3% w/w	4mg/ml	2.72mg/ml	9mg/ml	Enhance
Row 23	ND	ND	ND	ND	ND	ND
Row 24	ND	ND	ND	ND	ND	ND
Row 25	ND	ND	ND	ND	ND	ND
Row 26	ND	ND	ND	ND	ND	ND
Row 27	ND	ND	ND	ND	ND	ND
Row 28	ND	ND	ND	ND	ND	ND
Row 29	ND	ND	ND	ND	ND	ND

FIG. 2D
CONTINUED

Col. 1		Col. 2		Col. 3	Col. 4
BCS	II	II	III	III	III
Solubility	Practically insoluble <0.1 mg/ml	Very slightly soluble 0.1 - 1 mg/ml	Slightly soluble 1-10 mg/ml	Sparingly soluble 10 - 33 mg/ml	
Log P	Log P >2.5	Log P 1-2.5	Log P < 1	Log P < 1	
Surfactant (Hydrophilic) HLB >10	Enhance (adjust pH to increase solubility as required)	Enhance	No effect or Enhance	No effect	
Surfactant (Lipophilic) HLB <10	Inhibits	Inhibits	Enhance	No effect	
Bile Salt	Enhances (adjust pH to increase solubility as required)	Enhances	Enhances	No effect	
Micelles	Enhance (adjust pH to increase solubility as required)	Enhance	No effect or Enhance	No effect	
Fatty Acid	Enhance	Inhibits	No data	No data	
Counterion * Also consider API and counterions pKa	Enhance (adjusted pH as required)	Enhance (adjusted pH as required)	Enhance (adjusted pH as required)	Enhance n (adjusted pH as required)	
pH modifier * Also consider API pKa value	Enhance (adjust pH to increase solubility as required)	No data (Predict: Enhance via adjusting pH to increase solubility)	No data Predict: Enhance by increasing the unionized fraction Predict: Inhibits (by increasing the ionized fraction)	Enhance (by increasing the unionized fraction) Inhibits (by increasing the ionized fraction)	

FIG. 3

API	BCS class (sub class)	Mol wt (g/mol)	Water solubility (mg/ml)	log P	pKa	BCS classification sub groups
Carvedilol	2 (sub gp1)	406.5	0.0044	3.05	7.8 ; 15	BCS class II (Gp 1) Practically insoluble (<0.1mg/ml) Log P > 2.5
Piroxicam	2 (sub gp2)	331.4	0.143	2.2	5.1	BCS class II (Gp 2) Very slightly soluble (0.1 - 1mg/ml) Log P 1 - 2.5
Famotidine	3 (sub gp1)	337.5	1	-0.64	6.76	BCS class III (Gp 1) Slightly soluble (1 - 10mg/ml) Log P < 1
Atenolol	3 (sub gp2)	266.34	13.5	0.57	9.6	BCS class III (Gp 2) Sparsingly (10 - 33mg/ml) Log P < 1

FIG. 4

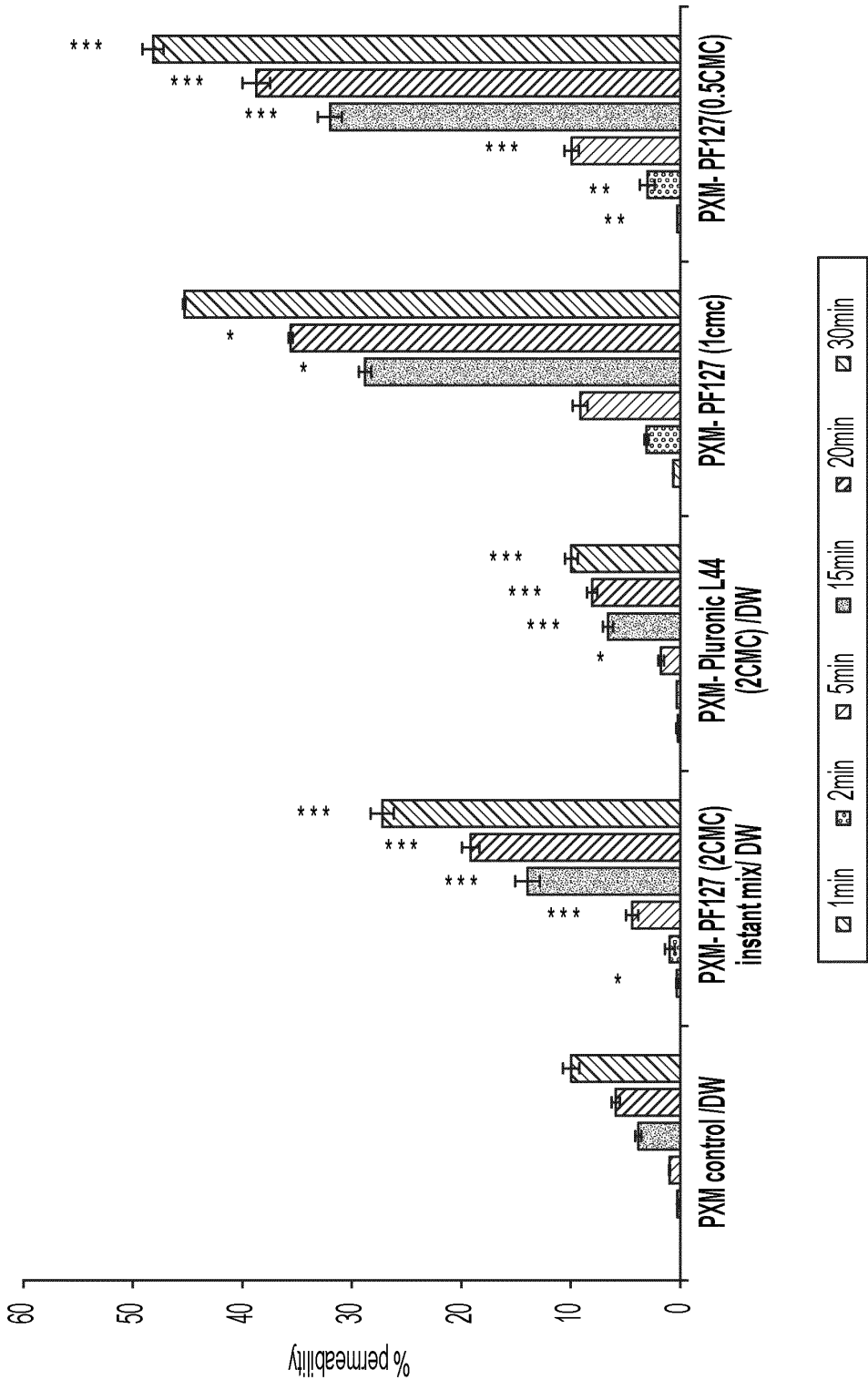


FIG. 5

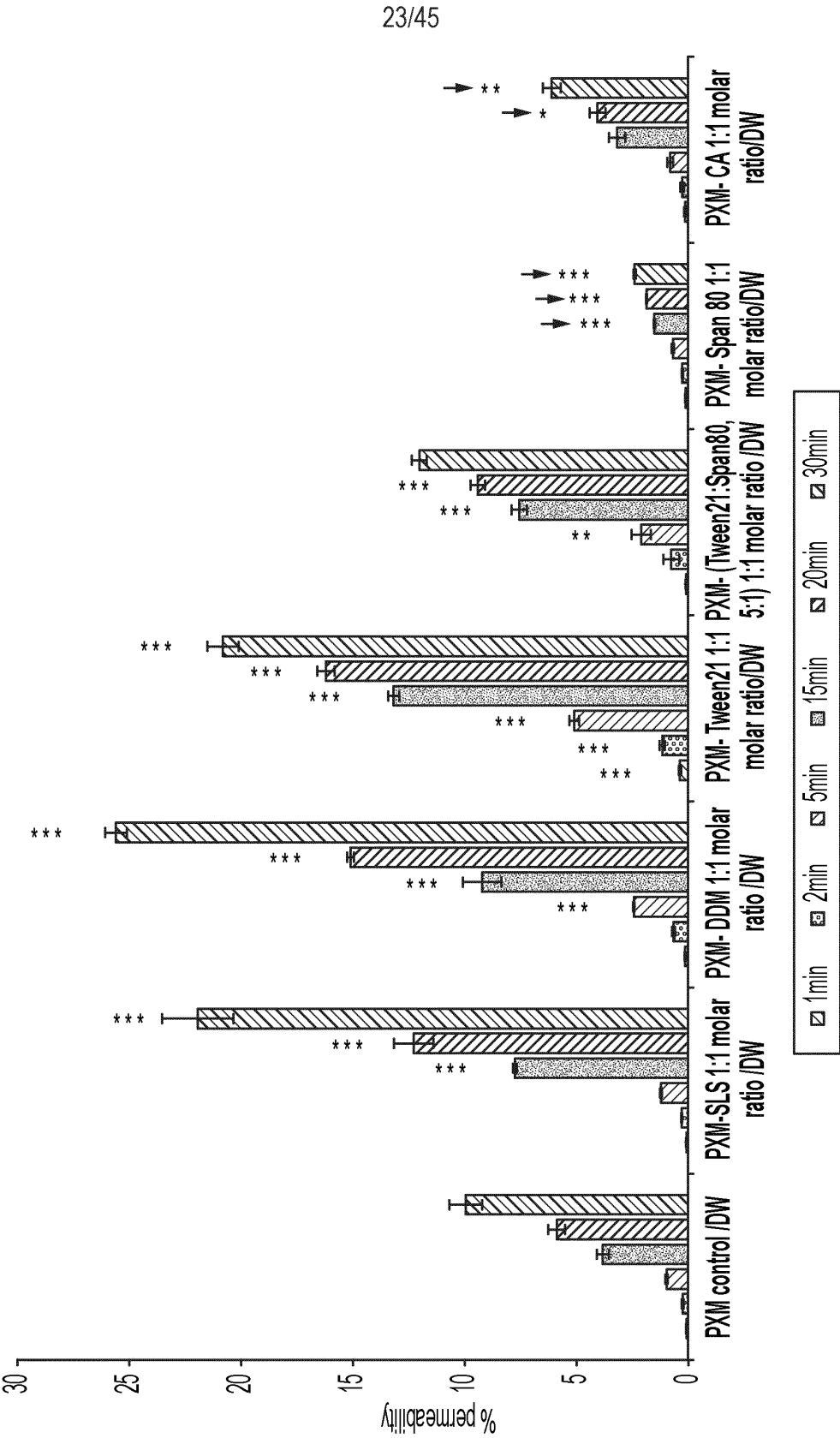


FIG. 6

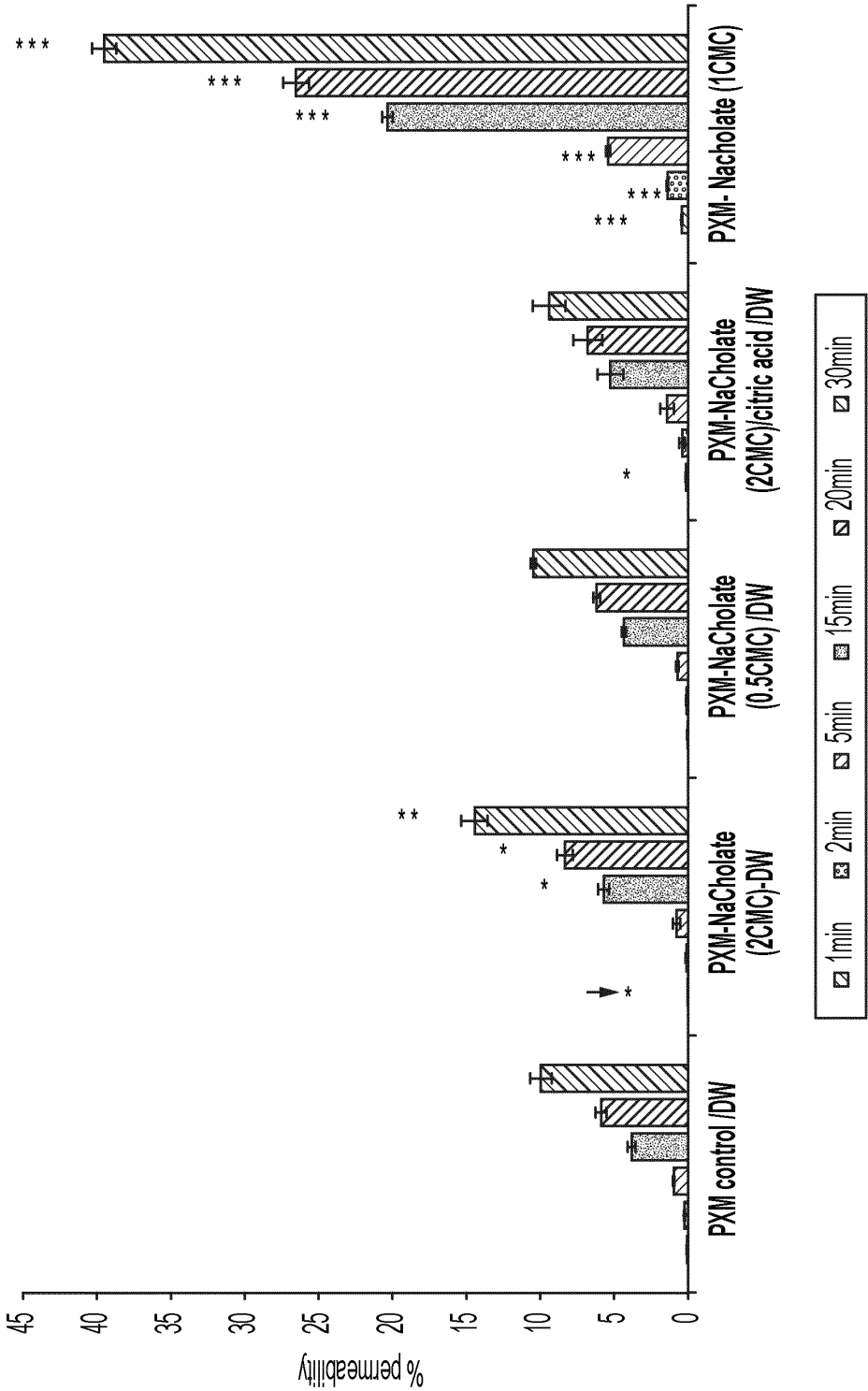


FIG. 7

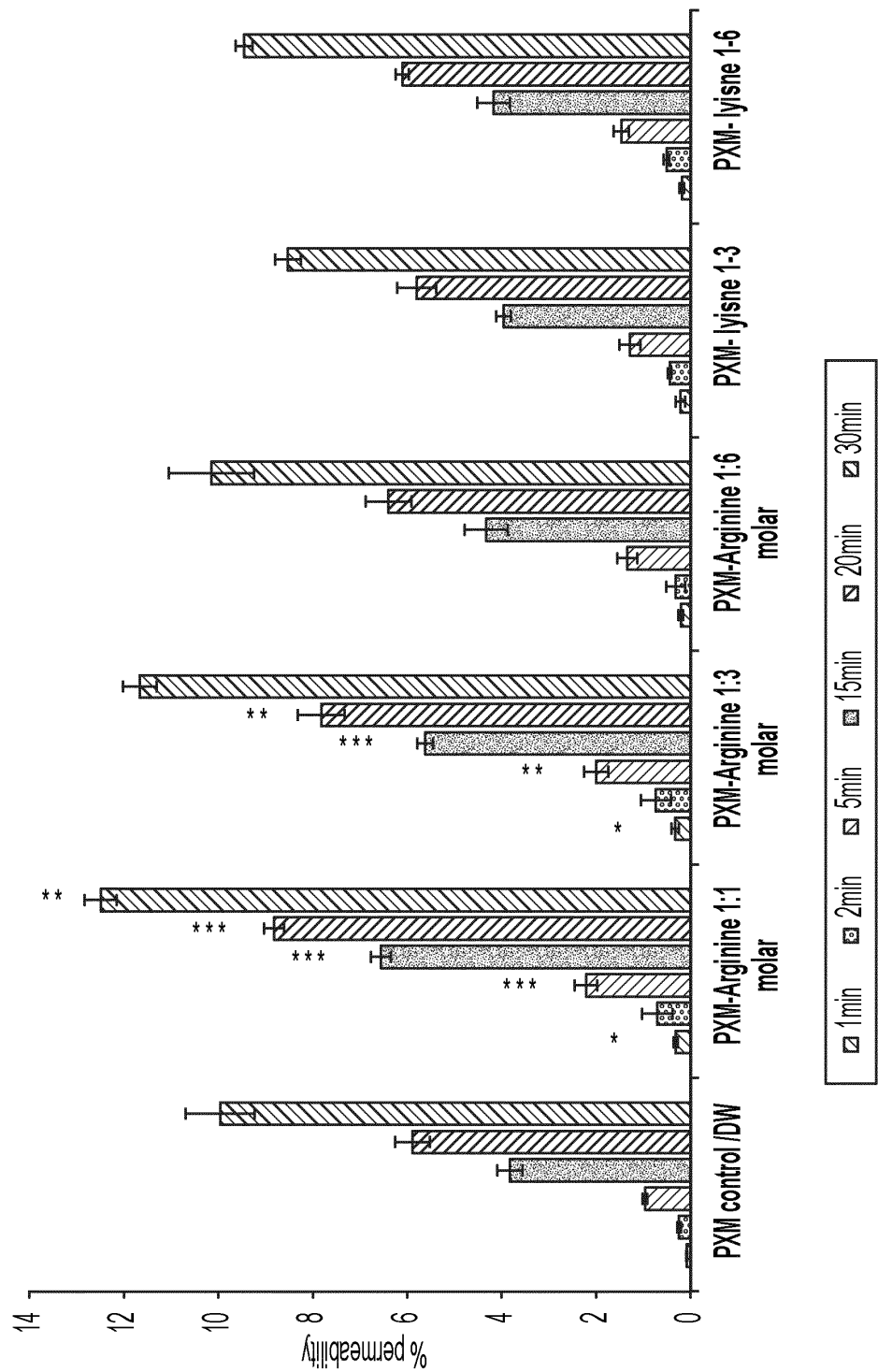


FIG. 8

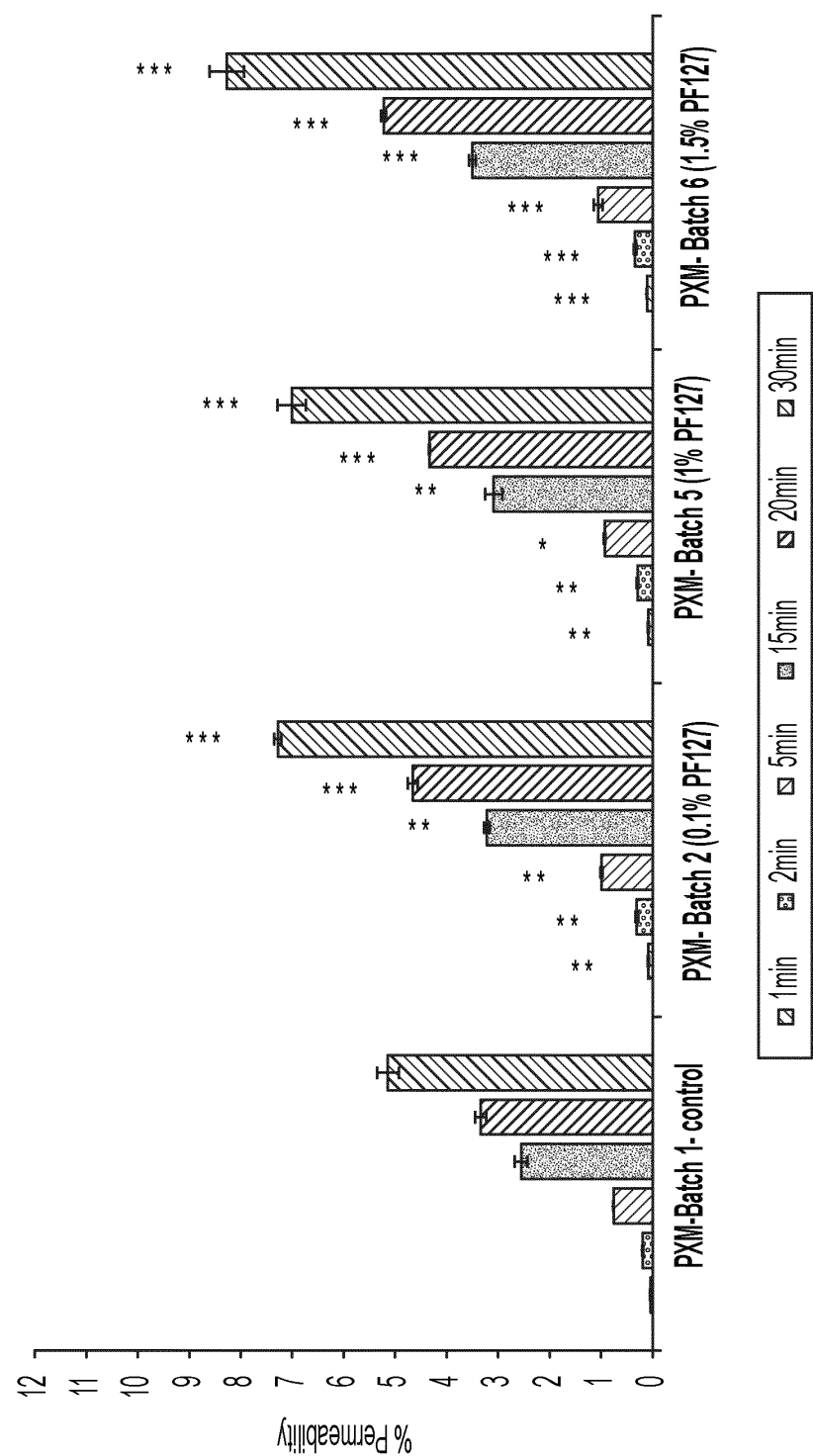


FIG. 9

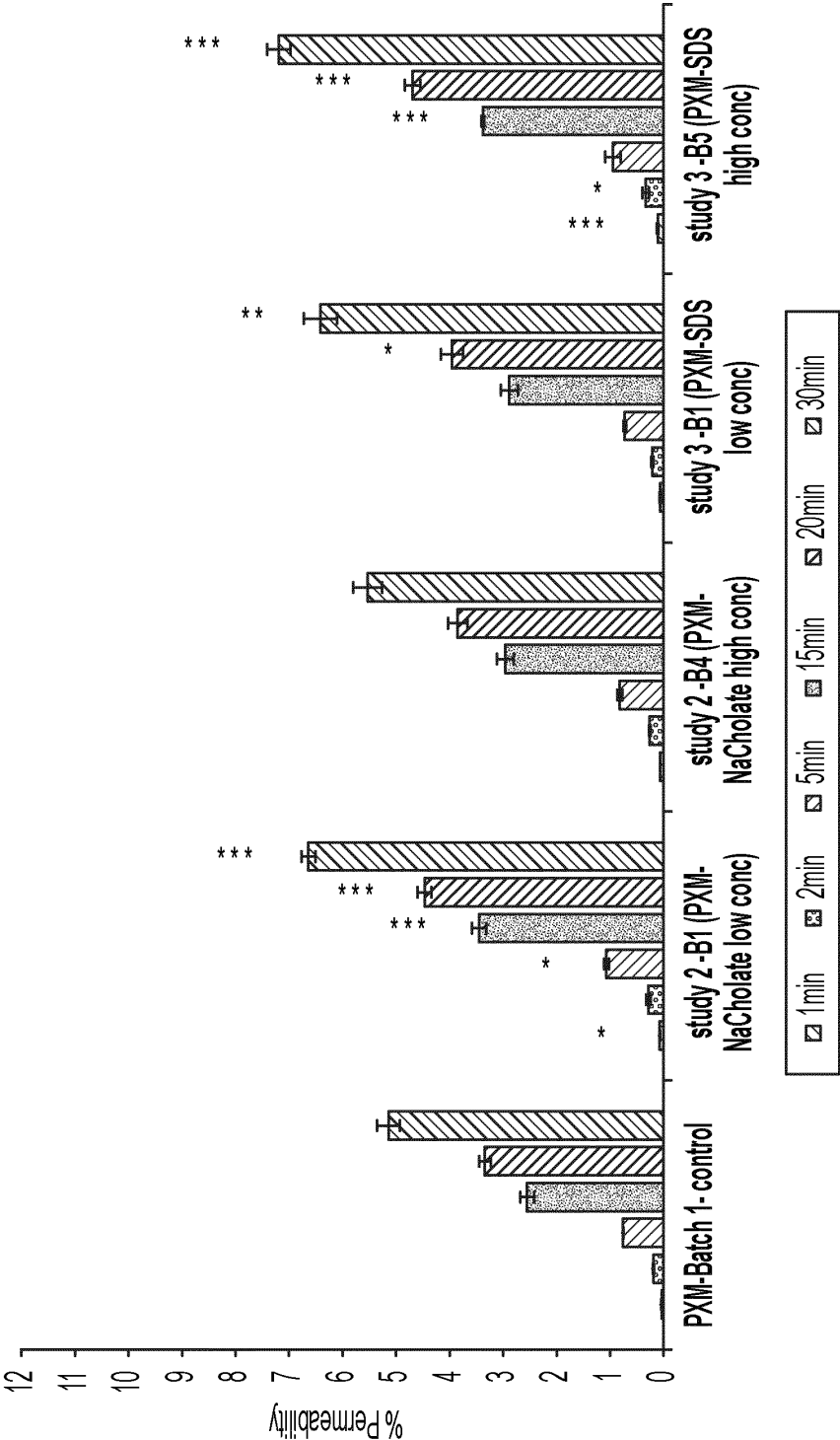


FIG. 10

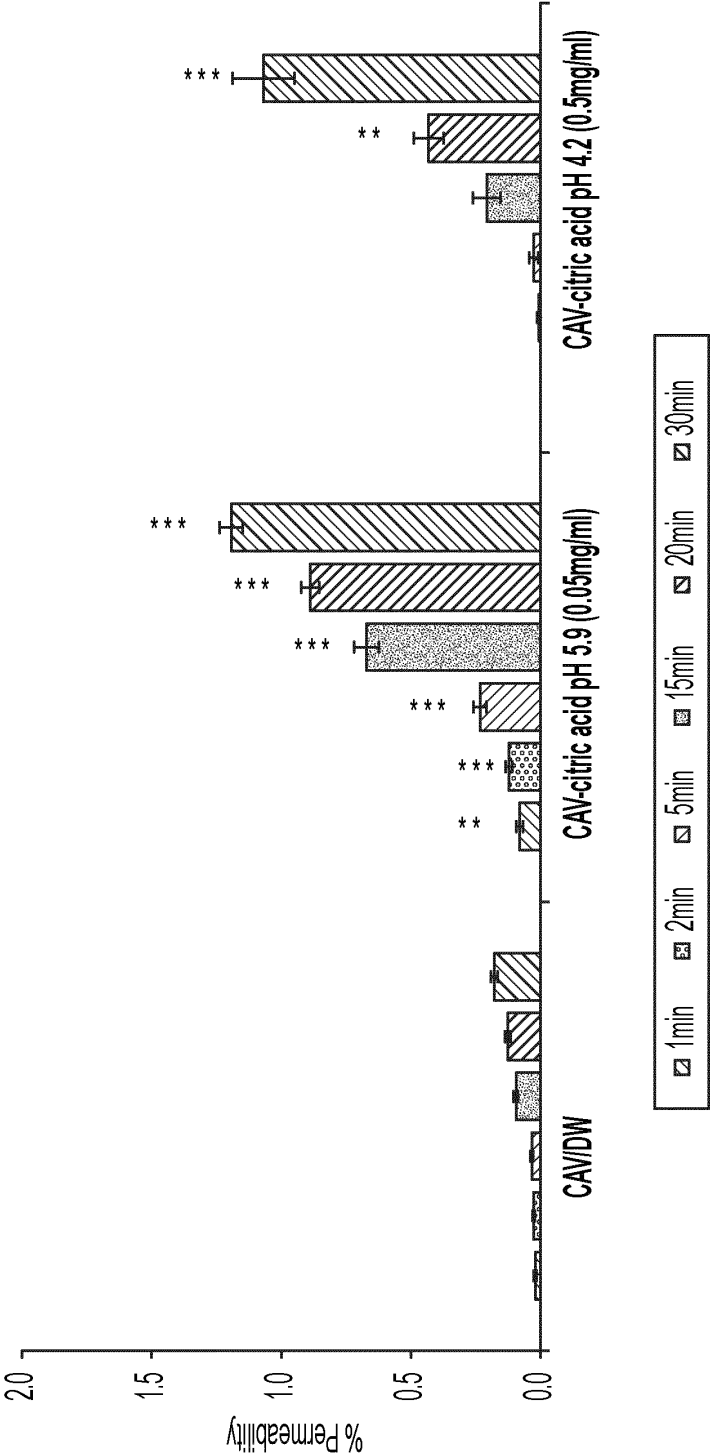


FIG. 11

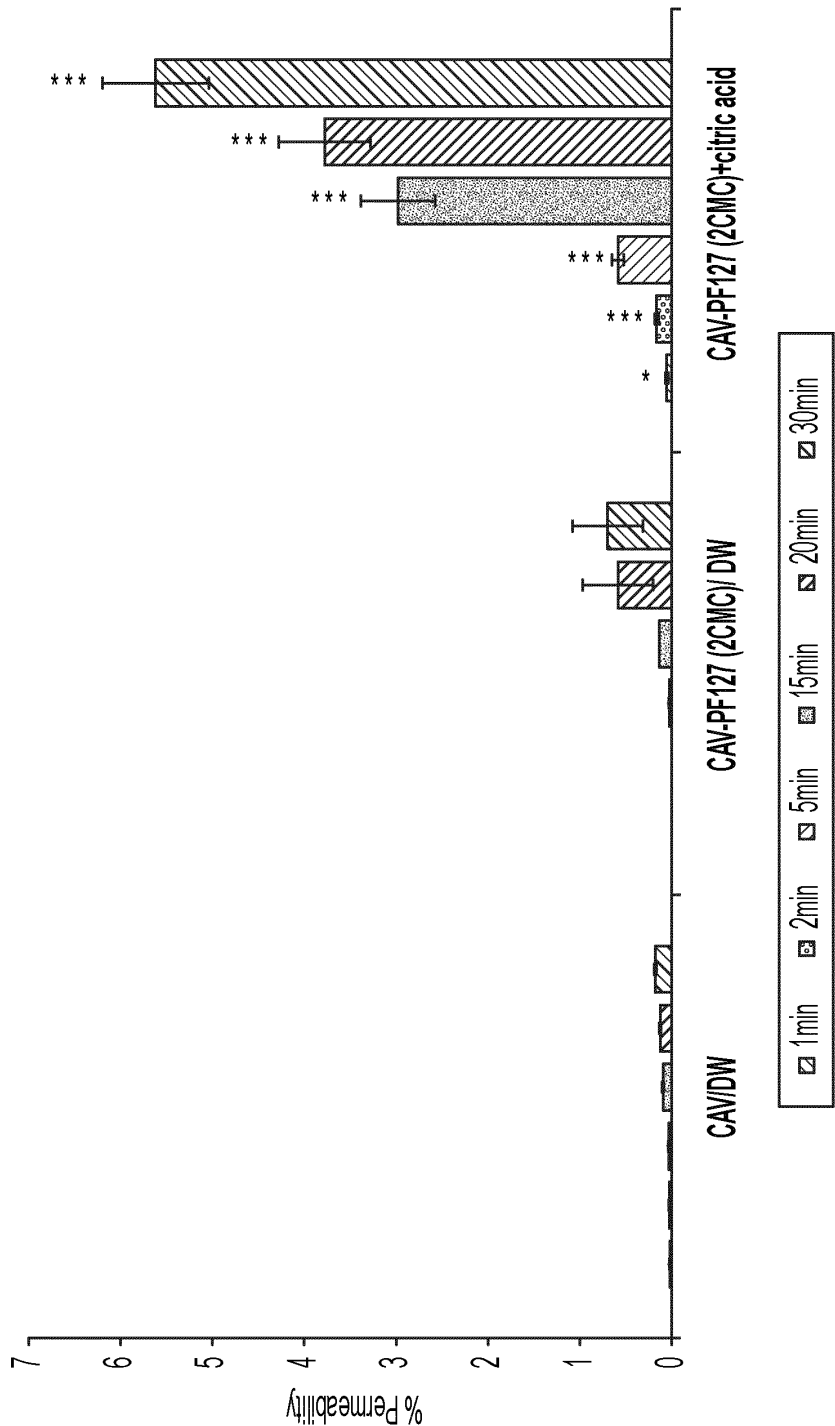


FIG. 12

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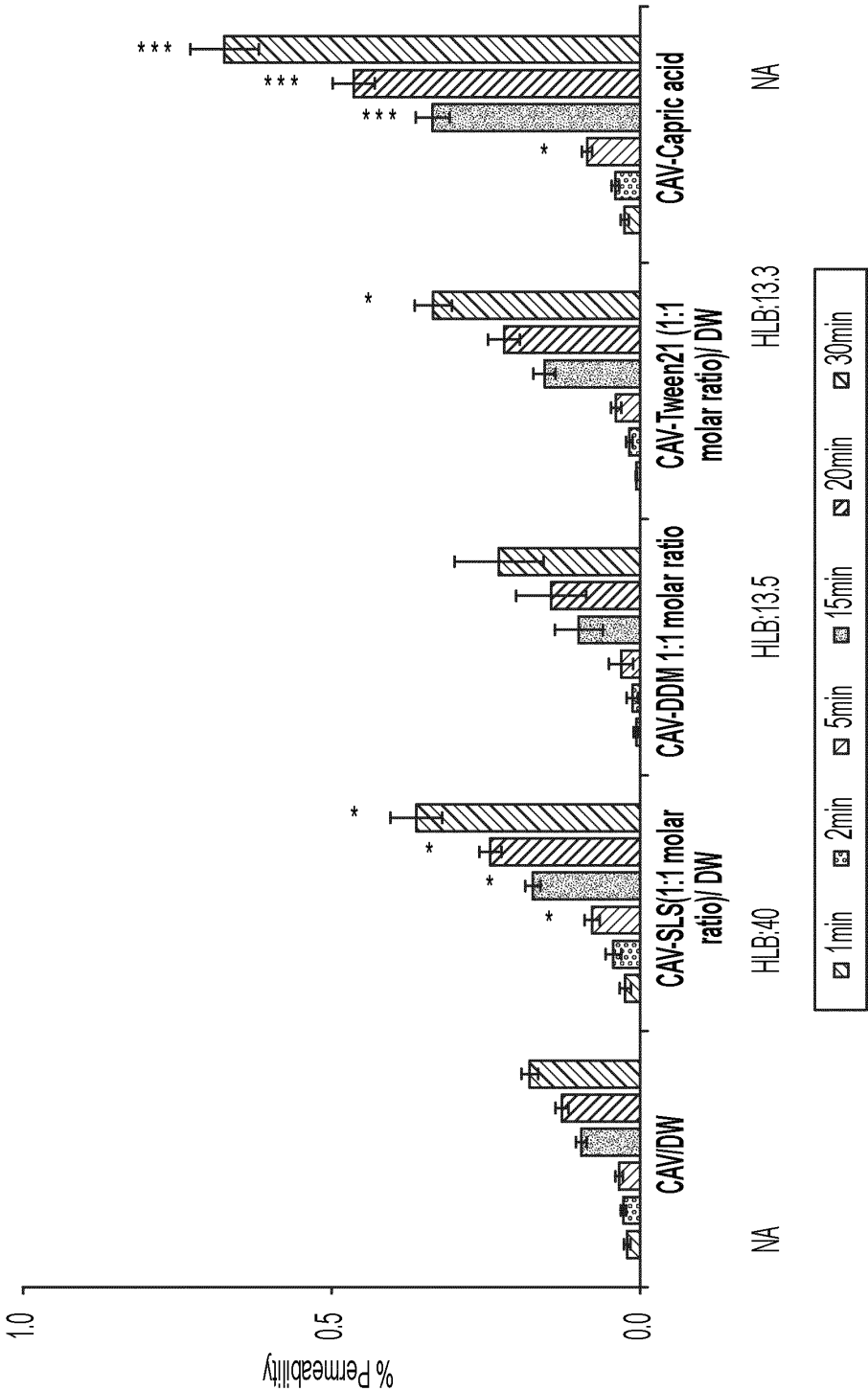


FIG. 13

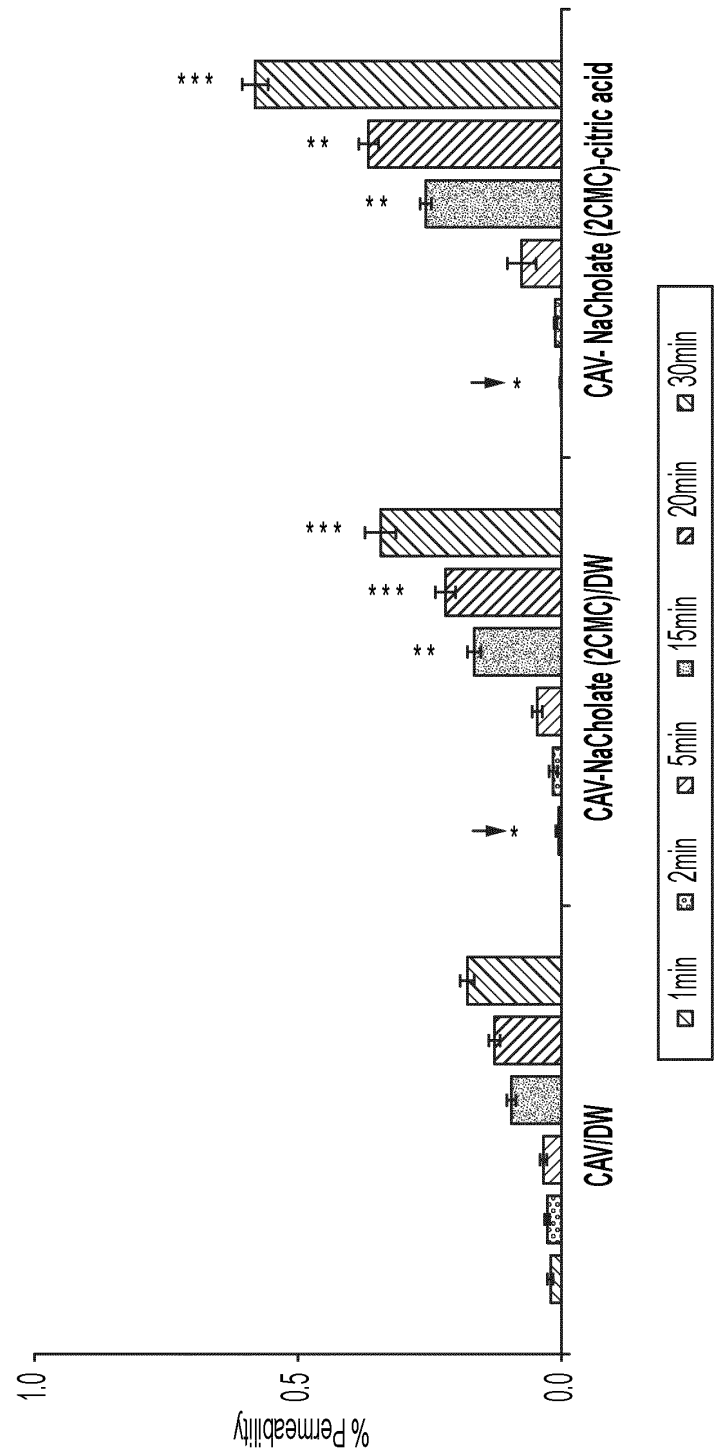


FIG. 14

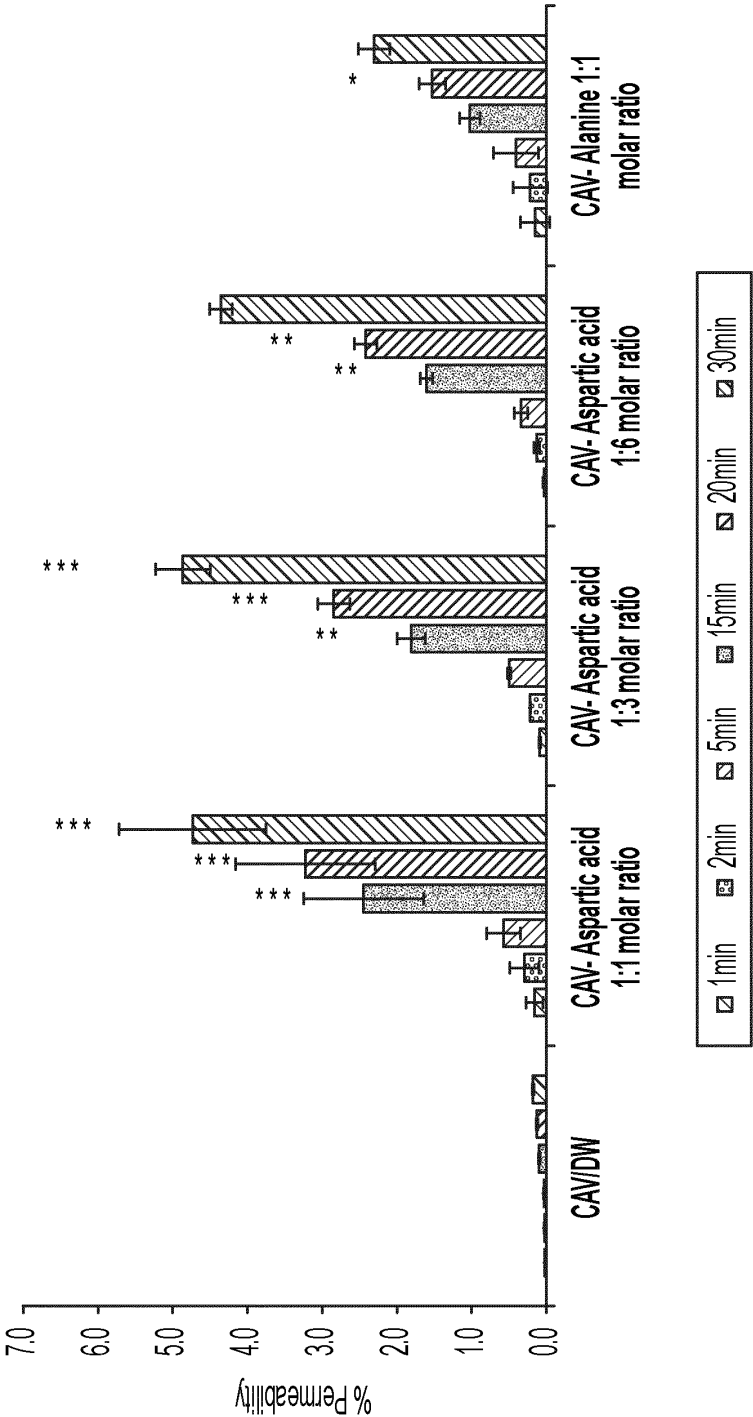


FIG. 15

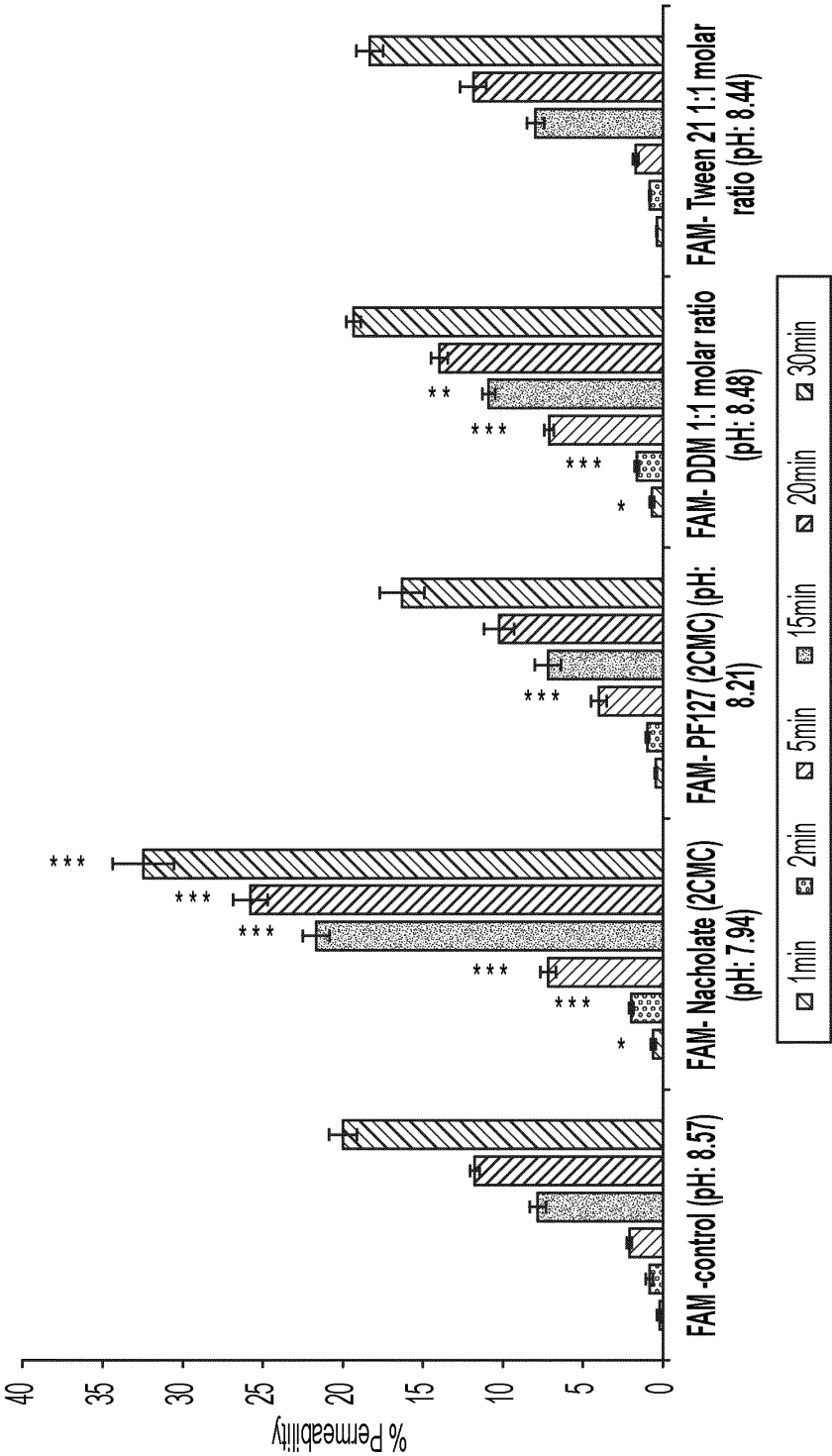


FIG. 16

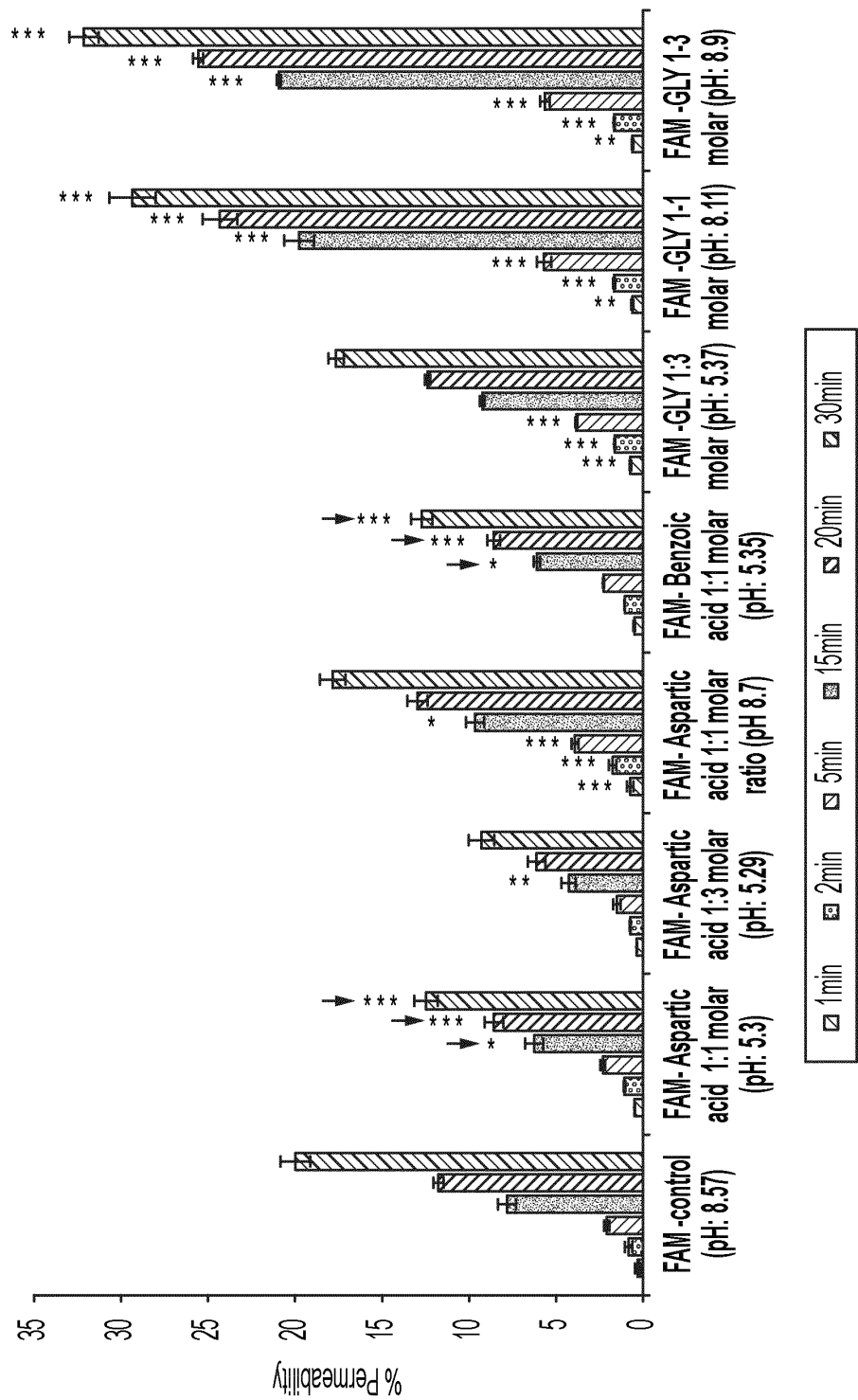


FIG. 17

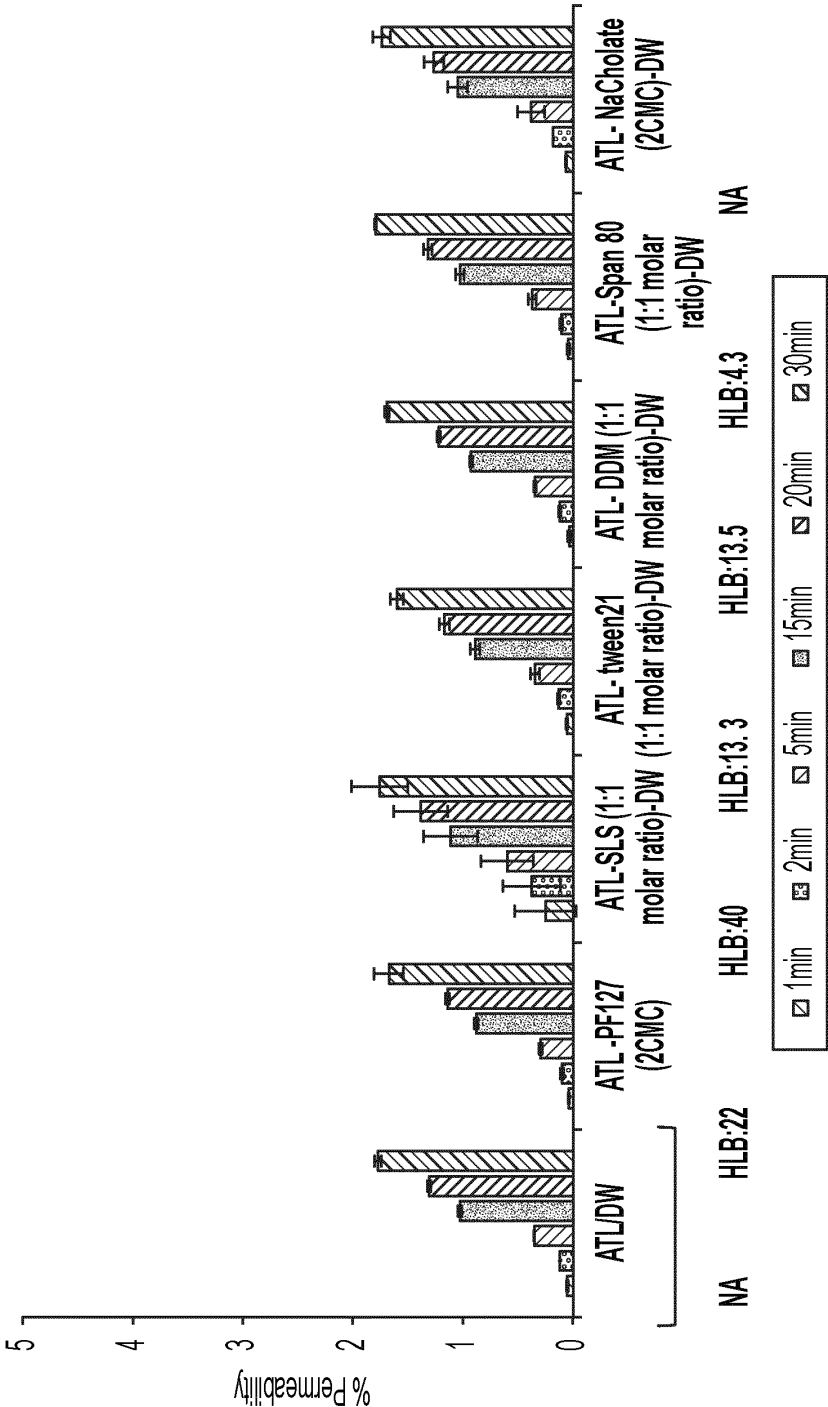


FIG. 18

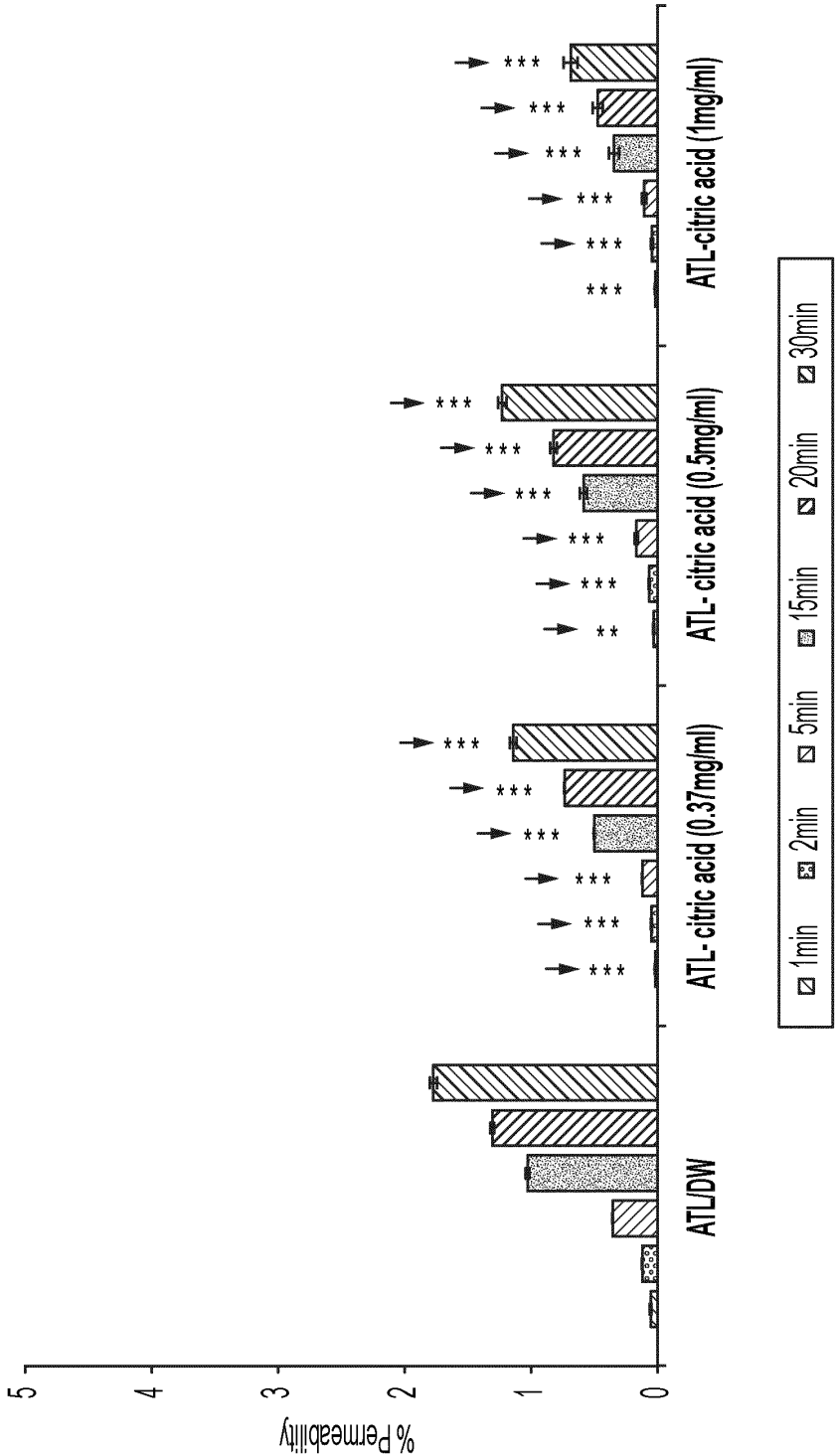


FIG. 19

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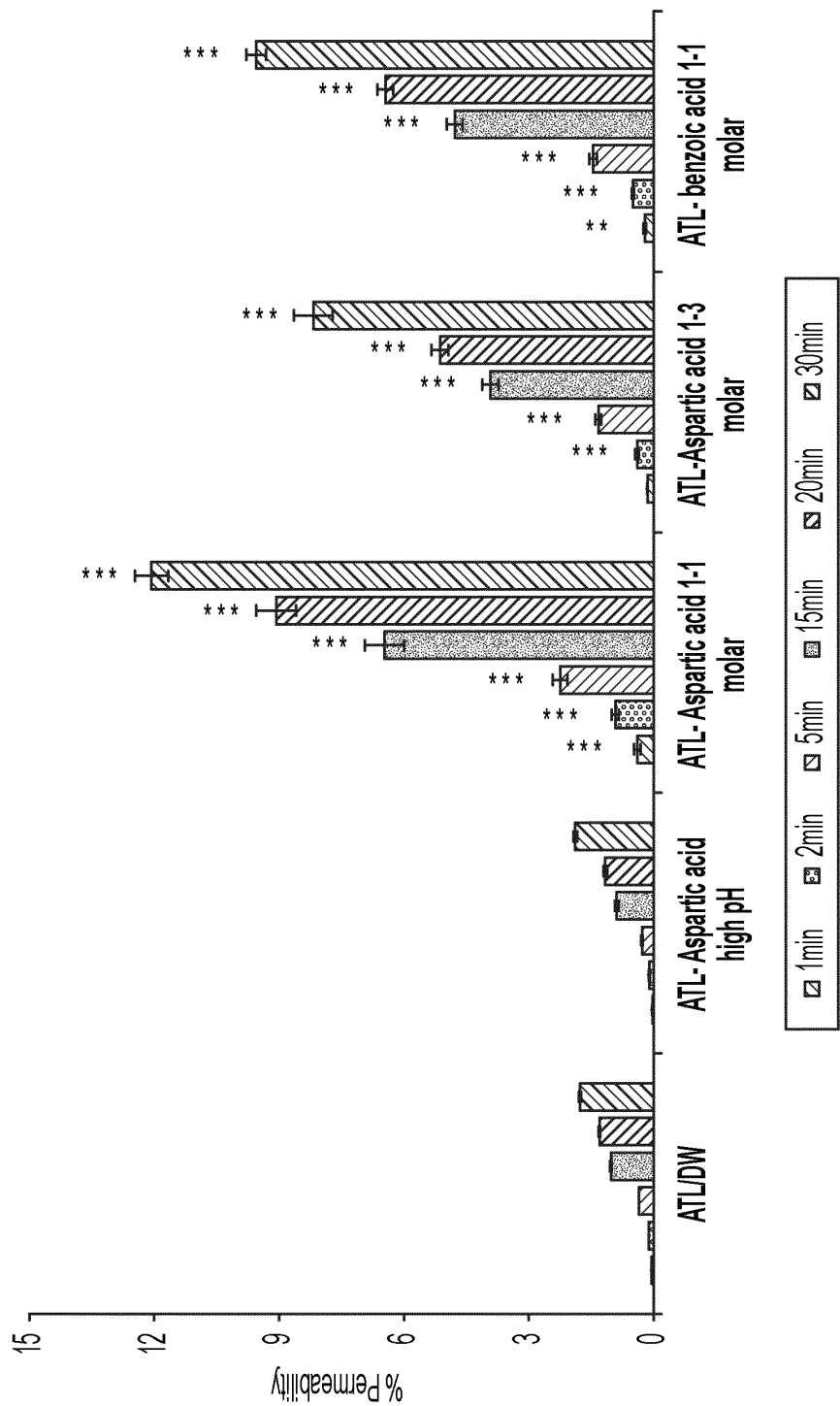


FIG. 20

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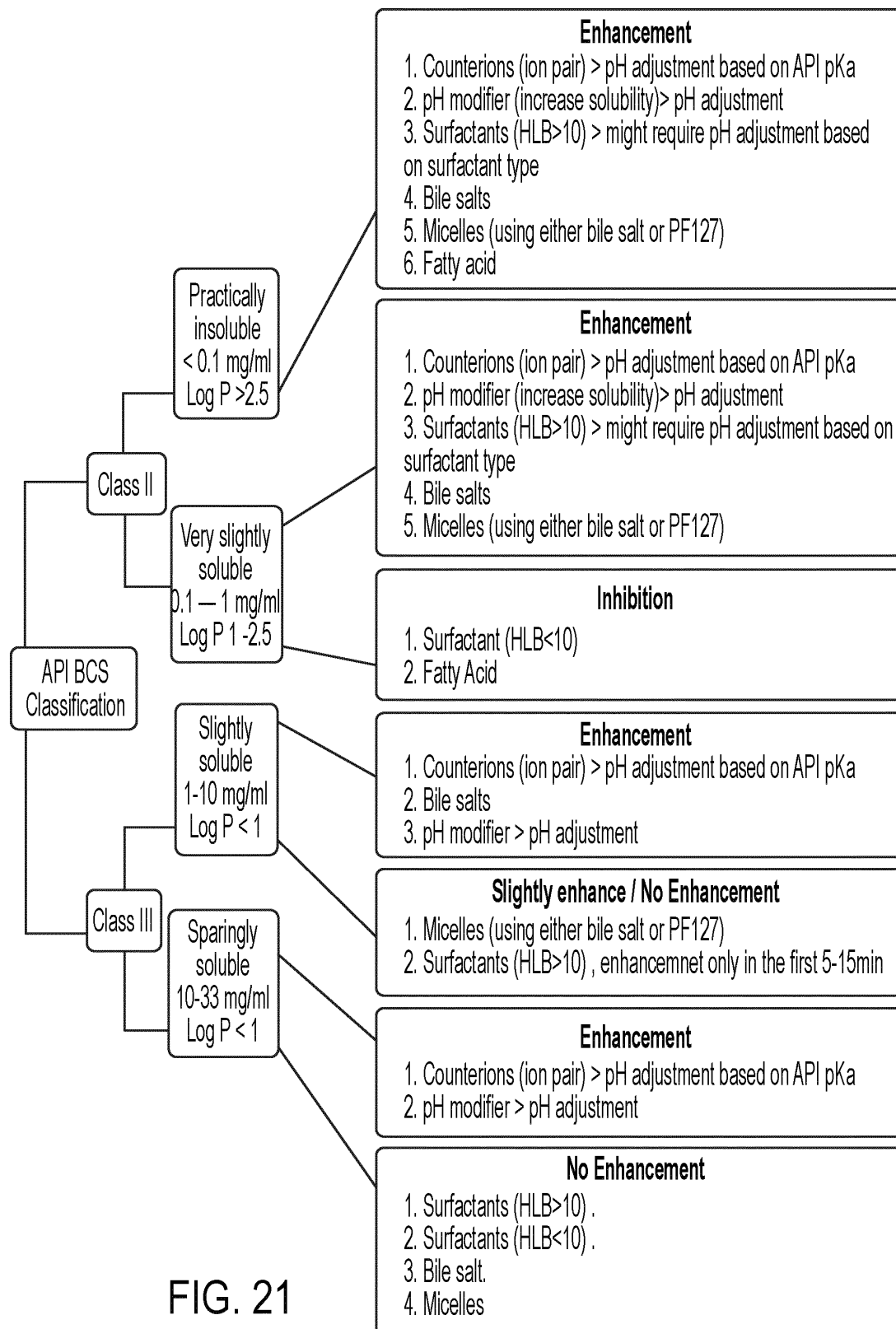


FIG. 21

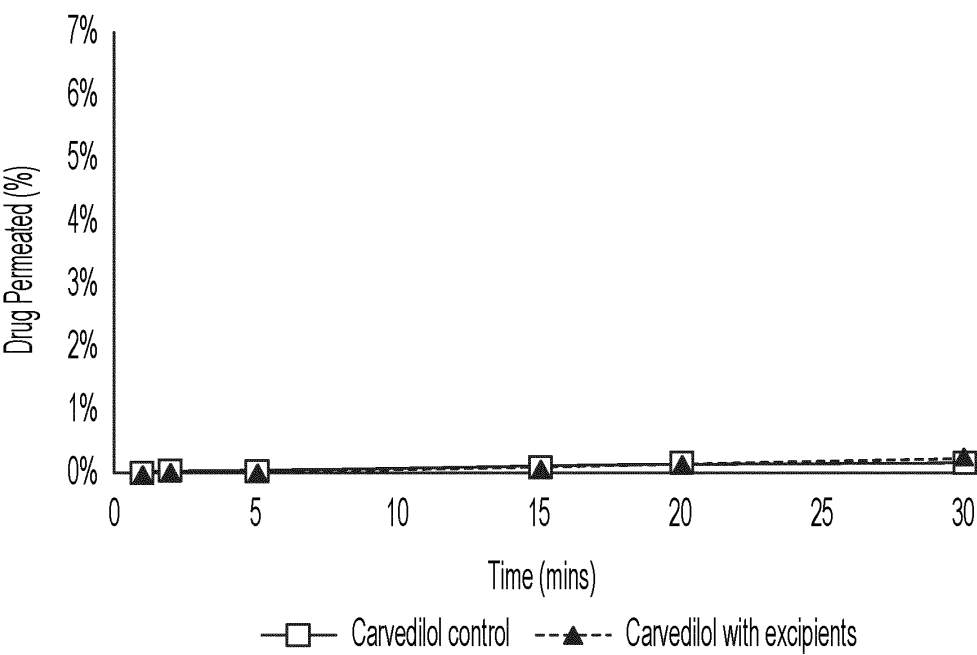


FIG. 22A

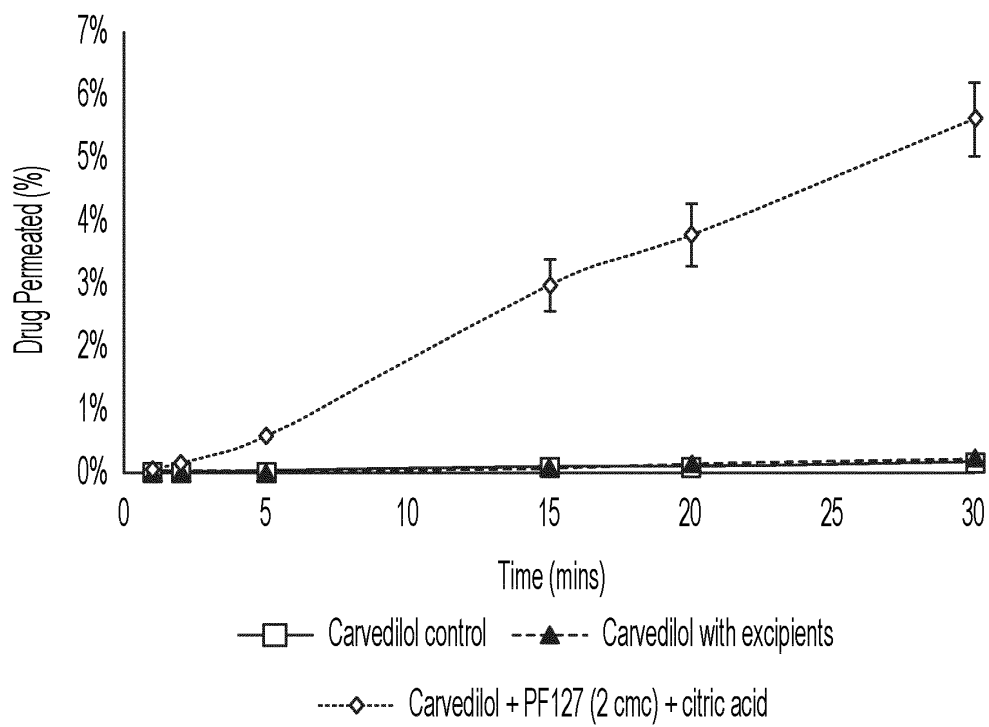


FIG. 22B

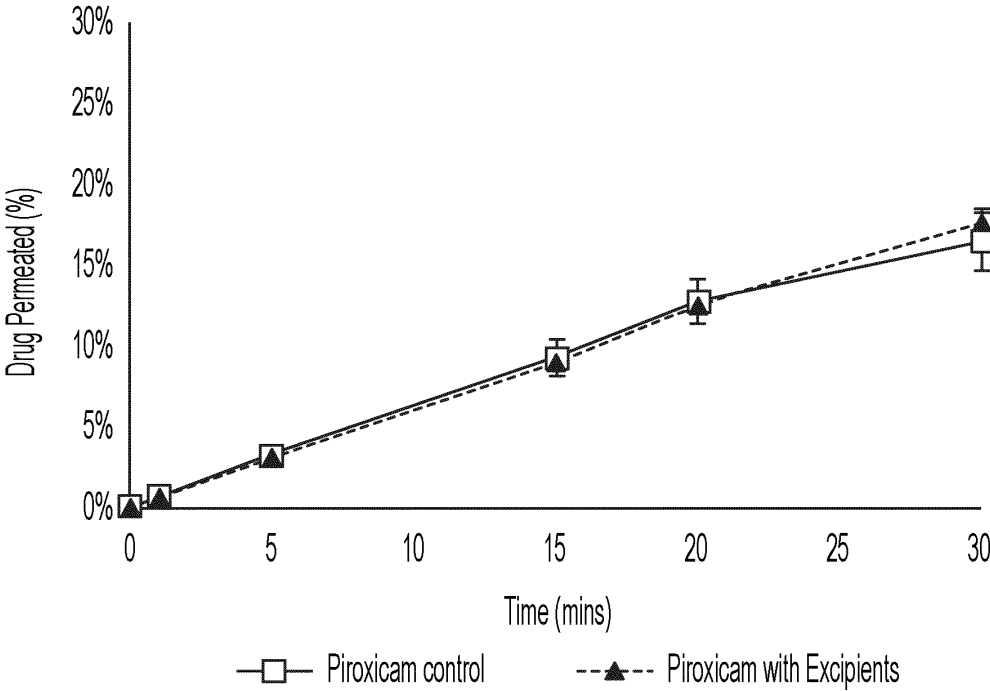


FIG. 22C

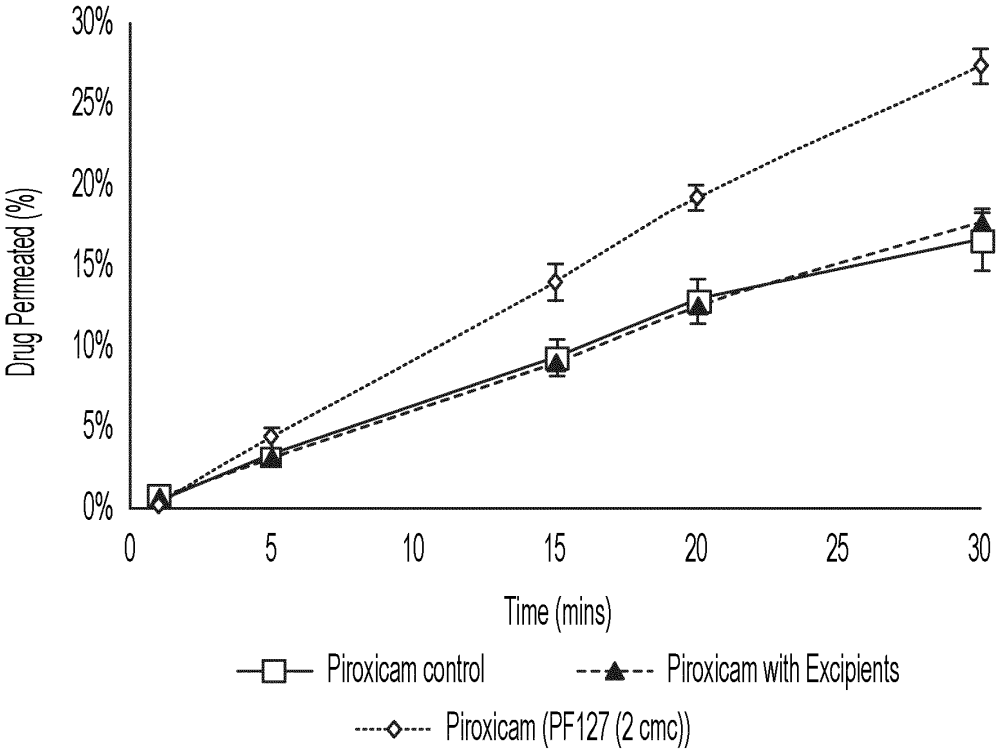


FIG. 22D

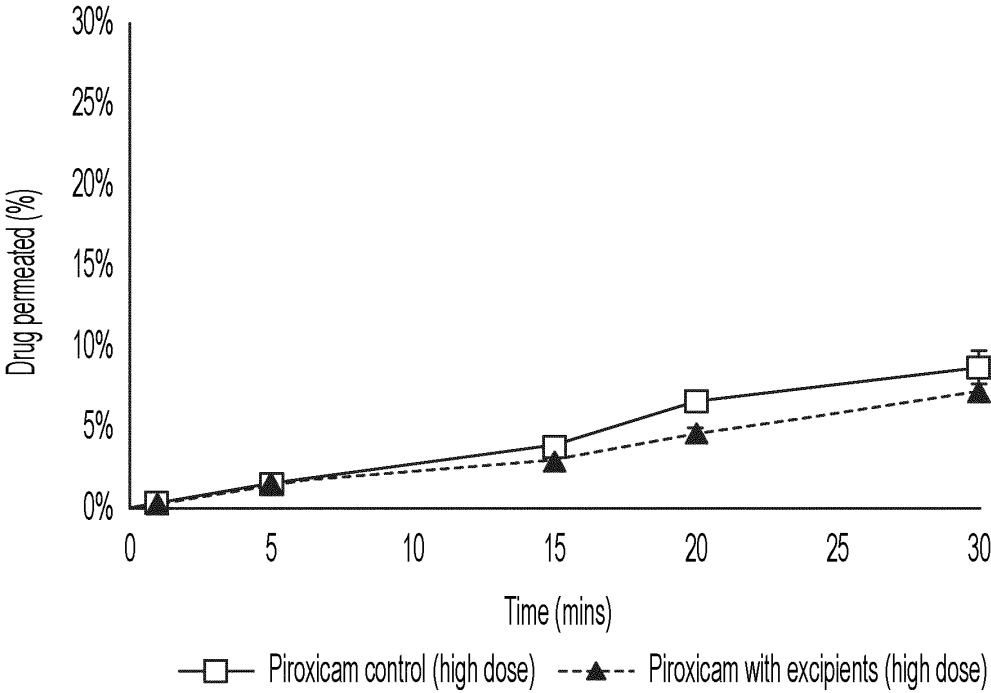


FIG. 22E

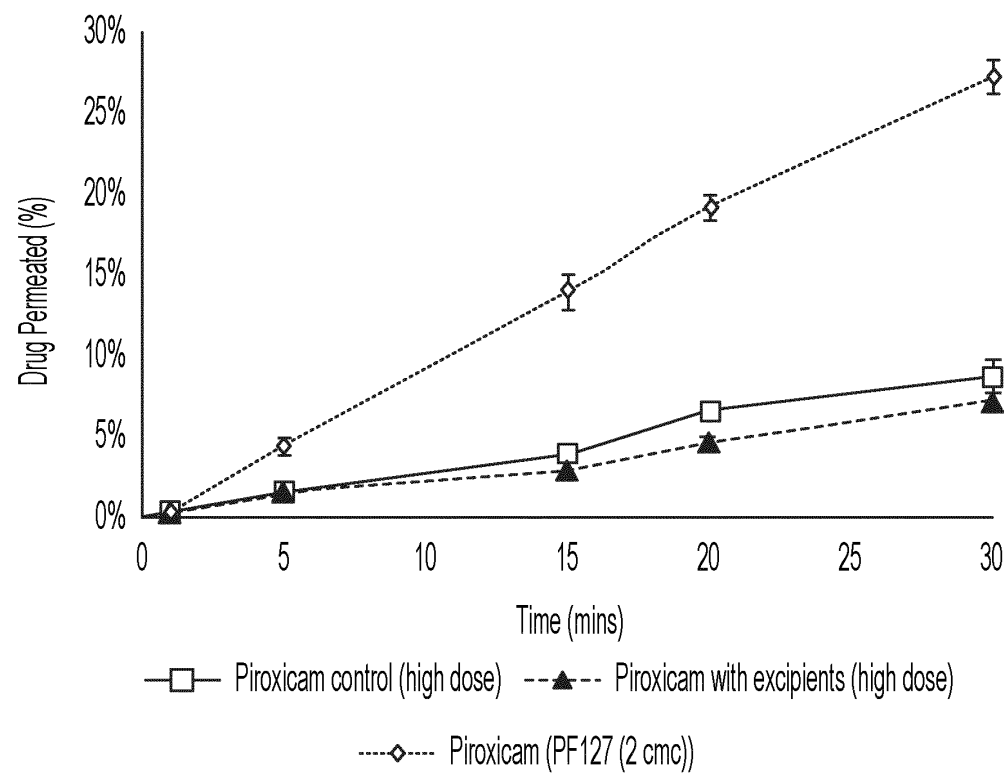


FIG. 22F

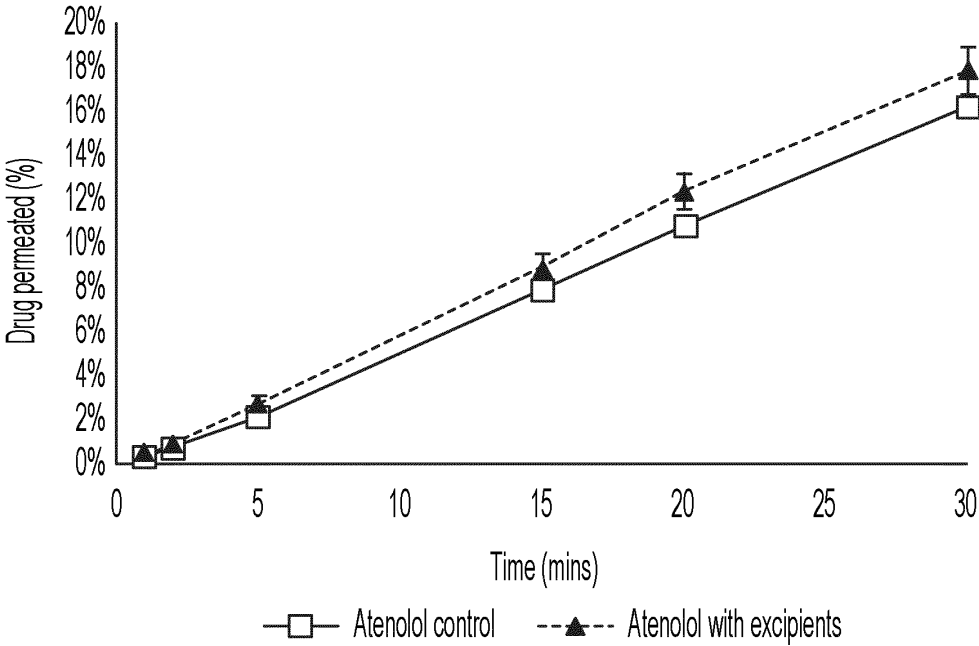


FIG. 22G