

Predicting neurological Adverse Drug Reactions based on biological, chemical and phenotypic properties of drugs using machine learning models

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Supplementary table 1 lists the features obtained after application of relief-based feature selection.

Biological		Phenotypic	Chemical
P24462	enzymes	C0919572	PubchemFP518
P20815		C1319200	PubchemFP148
P08684		C0281803	PubchemFP149
P10635		C0524662	PubchemFP336
P11712		C0919569	PubchemFP517
P05177		C0235524	PubchemFP422
P33261		C0857494	PubchemFP515
P10632		C0858765	PubchemFP300
P20813		C0860713	PubchemFP615
P05181		C0020440	PubchemFP3
P04798		C0231837	PubchemFP636
P11509		C1141861	PubchemFP682
P06276		C1619712	PubchemFP709
P23219		targets	C1510472
P35354	C0026650		PubchemFP688
P35348	C0036973		PubchemFP560
P08913	C0162297		PubchemFP430
P11229	C0026837		PubchemFP16
P04150	C0027066		PubchemFP593
P14416	C0206277		PubchemFP375
P14867	C0235063		PubchemFP657
P34903	C0855775		PubchemFP585
P47869	C0023066		PubchemFP646
P35367	C0011615		PubchemFP377
P31644	C0151828		PubchemFP600
Q16445	C0003578		PubchemFP356
P48169	C0013384		PubchemFP665
Q8N1C3	C0019521		PubchemFP495
P47870	C0497247		PubchemFP546
Q99928	C0235146		PubchemFP611
Q9UN88	C0233407		PubchemFP502
O14764	C0547030		PubchemFP569
P18507	C0340865		PubchemFP545
P78334	C0018790		PubchemFP439
P28472	C0006266		PubchemFP376
O00591	C0014591		PubchemFP645
P18505	C0013144		PubchemFP659
P28223	C0009782		PubchemFP437
P35368	C3665347		PubchemFP180
P07550	C0428977		PubchemFP628

P20309		C0015397	PubchemFP680
P08172		C0025061	PubchemFP633
P28335		C0018799	PubchemFP566
P08908		C0042373	PubchemFP449
P18089		C0004936	PubchemFP451
P08588		C0021053	PubchemFP689
P35372		C0085593	PubchemFP696
P18825		C0011991	PubchemFP549
P23975		C0003811	PubchemFP181
P21728		C0041657	PubchemFP341
P31645		C0041834	PubchemFP405
P41143		C0085631	PubchemFP299
P28221		C0010200	PubchemFP607
P28222		C0178298	PubchemFP393
P11388		C0344232	PubchemFP464
P08173		C0000737	PubchemFP579
P25100		C0687713	PubchemFP573
P03372		C0027765	PubchemFP143
P08912		C0020538	PubchemFP698
P41145		C0009676	PubchemFP619
P35462		C0037274	PubchemFP684
Q72547		C0036572	PubchemFP346
P10275		C0232462	PubchemFP578
Q14524		C0013395	PubchemFP603
Q01959		C0020458	PubchemFP618
P08183	transporters	C0009806	PubchemFP641
Q4U2R8		C0039231	PubchemFP552
Q9UNQ0		C0948594	PubchemFP668
P46059		C0917801	PubchemFP634
Q16348		C0002792	PubchemFP584
O15245		C0013404	PubchemFP677
P46721		C2830004	PubchemFP608
O15244		C0003123	PubchemFP595
Q92887		C0040034	PubchemFP520
Q9Y6L6		C0030554	PubchemFP470
Q8TCC7		C0231528	PubchemFP371
P33527		C0043352	PubchemFP391
O76082		C0020649	PubchemFP308
		C0017178	PubchemFP655
		C0036974	PubchemFP406
		C0231218	PubchemFP535
		C0003862	PubchemFP570
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		C2047937	PubchemFP574

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		C0009450	PubchemFP418
		C0039070	PubchemFP366
		C0008031	PubchemFP370
		C0234215	PubchemFP692
		C1443060	PubchemFP257
		C0233494	PubchemFP664
		C0023530	PubchemFP442
		C0027769	PubchemFP564
		C0004604	PubchemFP453
		C0013604	PubchemFP256
		C0040822	PubchemFP355
		C0002871	PubchemFP697
		C0042571	PubchemFP358
		C0016204	PubchemFP387
		C0037763	PubchemFP704
		C0030193	PubchemFP255
		C0040264	PubchemFP15
		C0002170	PubchemFP396
		C0002994	PubchemFP538
		C0035455	PubchemFP541
		C0162429	PubchemFP381
		C0031350	PubchemFP606
		C0015967	PubchemFP498
		C0041969	PubchemFP651
		C0042075	PubchemFP403
		C0085649	PubchemFP506
		C0014742	PubchemFP472
		C0042109	PubchemFP482
		C0037199	PubchemFP656
		C0013378	PubchemFP617
		C0242350	PubchemFP643
		C0042023	PubchemFP443
		C0162830	PubchemFP340
		C0018524	PubchemFP683
		C0038362	PubchemFP523
		C0001824	PubchemFP382
		C0851353	PubchemFP186
		C0009763	PubchemFP678
		C0019158	PubchemFP660
		C0267792	PubchemFP640
		C0032285	PubchemFP555
		C0038325	PubchemFP613

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		C0042029	PubchemFP594
		C0518015	PubchemFP179
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		C0851341	PubchemFP592
		C0004093	PubchemFP542
		C0020580	PubchemFP553
		C0018965	PubchemFP710
		C0020456	PubchemFP524
		C0027947	PubchemFP712
		C0043096	PubchemFP392
		C0006277	PubchemFP604
		C0013428	PubchemFP599
		C0948089	PubchemFP185
		C0027051	PubchemFP540
		C0855242	PubchemFP556
		C0017152	PubchemFP490
		C0038990	PubchemFP530
		C0011124	PubchemFP516
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		C0085633	PubchemFP434
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		C0006145	PubchemFP373
		C1306341	PubchemFP441
		C0041912	PubchemFP491
		C0026826	PubchemFP333
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		C0012569	PubchemFP416
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		C0024902	PubchemFP547
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			PubchemFP483

Supplementary table 2 mentions the different percentages at which the under-sampled class was over-sampled using SMOTE method.

Neurological ADR	SMOTE % (final %age used is in bold)					
Arteritic anterior ischaemic optic neuropathy	100	150	200	250	300	
Autonomic neuropathy	50	100	150	200	250	300
Neuromuscular block prolonged	50	100	150	200	250	290
Neuralgia	1000					
Neuritis	1000					
Neuropathy	500					
Neuromyopathy	50	100	150	200	250	300
Neurologic reaction	1000	1100				
Neurosis	2500					
Neurotoxicity	2500					
Neurological impairment	50	100	150	200	250	300
Neuroleptic malignant syndrome	1500					
Neuropathy peripheral	400					
Neuritis retrobulbar	300					
Neurological symptom	4500					
Nervous system disorder	Balanced					
Optic neuritis	2000					
Post herpetic neuralgia	100	150	200	250	300	
Peripheral motor neuropathy	6500					
Polyneuropathy	4000					
Peripheral sensory neuropathy	3000					
Peripheral sensorimotor neuropathy	50	100	150	200	250	300

Supplementary table 3 provides the performances of the models generated using the three levels of features, biological, chemical, and phenotypic and their combination using the imbalanced data as input without applying SMOTE technique.

Modelling using Biological features

	Accuracy (%)	Precision	Recall	F-score	AUC
Arteritic anterior ischaemic optic neuropathy	99.45	0.99	1	0.99	0.50
Autonomic neuropathy	99.45	0.99	1	0.99	0.50
Nervous system disorder	59.5	0.60	0.86	0.70	0.55
Neuralgia	91.25	0.91	0.99	0.95	0.49
Neuritis	93.98	0.93	1	0.96	0.6
Neuritis retrobulbar	91.8	0.92	0.99	0.95	0.49
Neuroleptic malignant syndrome	94.5	0.94	1	0.97	0.50
Neurologic reaction	98.9	0.98	1	0.99	0.50
Neurological impairment	99.45	0.99	1	0.99	0.50
Neurological symptom	97.8	0.97	1	0.98	0.50
Neuromuscular block prolonged	99.45	0.99	1	0.99	0.50
Neuromyopathy	99.45	0.99	1	0.99	0.50
Neuropathy	86.88	0.86	1	0.93	0.50
Neuropathy peripheral	83.60	0.83	1	0.91	0.50
Neurosis	96.17	0.96	1	0.98	0.50
Neurotoxicity	96.17	0.96	1	0.98	0.50
Optic neuritis	95.62	0.95	1	0.97	0.50
Peripheral motor neuropathy	98.90	0.98	1	0.99	0.50
Peripheral sensorimotor neuropathy	99.45	0.99	1	0.99	0.50
Peripheral sensory neuropathy	97.26	0.97	1	0.98	0.50
Polyneuropathy	97.81	0.97	1	0.98	0.50
Post herpetic neuralgia	99.45	0.99	1	0.99	0.50

Modelling using Chemical features

	Accuracy (%)	Precision	Recall	F-score	AUC
Arteritic anterior ischaemic optic neuropathy	98.90	0.99	0.99	0.99	0.49
Autonomic neuropathy	99.45	0.99	1	0.99	0.50
Nervous system disorder	64.48	0.67	0.73	0.70	0.63
Neuralgia	89.61	0.92	0.97	0.94	0.51
Neuritis	90.16	0.92	0.97	0.94	0.52
Neuritis retrobulbar	99.45	0.99	1	0.99	0.5
Neuroleptic malignant syndrome	94.53	0.96	0.97	0.97	0.68
Neurologic reaction	98.36	0.98	0.99	0.99	0.49
Neurological impairment	98.90	0.99	0.99	0.99	0.49
Neurological symptom	96.17	0.97	0.98	0.98	0.49
Neuromuscular block prolonged	99.45	0.99	1	0.99	0.50
Neuromyopathy	99.45	0.99	1	0.99	0.50
Neuropathy	78.14	0.87	0.88	0.87	0.50
Neuropathy peripheral	75.40	0.85	0.85	0.85	0.54
Neurosis	94.53	0.96	0.97	0.97	0.56
Neurotoxicity	92.89	0.97	0.95	0.96	0.62
Optic neuritis	93.44	0.96	0.97	0.96	0.54
Peripheral motor neuropathy	98.36	0.98	0.99	0.99	0.49
Peripheral sensorimotor neuropathy	99.45	0.99	1	0.99	0.50
Peripheral sensory neuropathy	96.17	0.97	0.98	0.98	0.49
Polyneuropathy	96.17	0.97	0.98	0.98	0.49
Post herpetic neuralgia	98.90	1	0.98	0.99	0.99

Modelling using Phenotypic features

	Accuracy (%)	Precision	Recall	F-score	AUC
Arteritic anterior ischaemic optic neuropathy	99.45	0.99	1	0.99	0.50
Autonomic neuropathy	98.36	0.99	0.98	0.99	0.49
Nervous system disorder	87.43	0.92	0.84	0.88	0.87
Neuralgia	88.52	0.93	0.94	0.93	0.57
Neuritis	89.07	0.92	0.96	0.94	0.48
Neuritis retrobulbar	99.45	0.99	1	0.99	0.50
Neuroleptic malignant syndrome	92.89	0.94	0.97	0.96	0.53
Neurologic reaction	99.45	0.99	1	0.99	0.75
Neurological impairment	99.45	0.99	1	0.99	0.50
Neurological symptom	97.81	0.97	1	0.98	0.50
Neuromuscular block prolonged	99.45	0.99	1	0.99	0.50
Neuromyopathy	99.45	0.99	1	0.99	0.50
Neuropathy	86.33	0.90	0.93	0.92	0.65
Neuropathy peripheral	80.32	0.86	0.90	0.88	0.58
Neurosis	95.0	0.97	0.97	0.97	0.63
Neurotoxicity	94.53	0.96	0.97	0.97	0.56
Optic neuritis	94.5	0.95	0.98	0.97	0.49
Peripheral motor neuropathy	98.90	0.98	1	0.99	0.50
Peripheral sensorimotor neuropathy	98.90	0.99	0.99	0.99	0.49
Peripheral sensory neuropathy	94.53	0.97	0.97	0.97	0.48
Polyneuropathy	96.72	0.97	0.98	0.98	0.49
Post herpetic neuralgia	100	1	1	1	1

Modelling using Merged features

	Accuracy (%)	Precision	Recall	F-score	AUC
Arteritic anterior ischaemic optic neuropathy	99.45	0.99	1	0.99	0.50
Autonomic neuropathy	99.45	0.99	1	0.99	0.50
Nervous system disorder	79.78	0.83	0.80	0.82	0.79
Neuralgia	85.79	0.93	0.90	0.92	0.61
Neuritis	90.71	0.93	0.96	0.95	0.58
Neuritis retrobulbar	99.45	0.99	1	0.99	0.50
Neuroleptic malignant syndrome	93.98	0.96	0.97	0.96	0.68
Neurologic reaction	99.45	0.99	1	0.99	0.75
Neurological impairment	99.45	0.99	1	0.99	0.50
Neurological symptom	96.72	0.97	0.98	0.98	0.49
Neuromuscular block prolonged	99.45	0.99	1	0.99	0.50
Neuromyopathy	99.45	0.99	1	0.99	0.50
Neuropathy	81.42	0.90	0.88	0.89	0.62
Neuropathy peripheral	80.87	0.88	0.88	0.88	0.64
Neurosis	93.98	0.97	0.96	0.96	0.69
Neurotoxicity	93.98	0.97	0.96	0.96	0.69
Optic neuritis	93.44	0.96	0.96	0.96	0.60
Peripheral motor neuropathy	98.36	0.98	0.99	0.99	0.49
Peripheral sensorimotor neuropathy	99.45	0.99	1	0.99	0.50
Peripheral sensory neuropathy	96.17	0.97	0.98	0.98	0.49
Polyneuropathy	97.81	0.97	1	0.98	0.50
Post herpetic neuralgia	99.45	1	0.99	0.99	0.99