

DINTO-Graph inference report

This document presents a detailed report of the results of the inferential process on DINTO-Graph. First of all, it shows the description of the 59 rules composing the first set of SWRL rules, 33 of which went on to be featured in the final version of DINTO-Graph. Afterwards, the succession of adjustments leading to the final set of rules carrying out the inferences is summarised. Finally, a comprehensive table explains some statistics of the inferential process arranged by inferences by drug families.

1 DINTO's rules of inference (first ruleset)

Figure 1 shows SWRL rules 1-30 of the first ruleset as developed in DINTO.

1	activates(?othery, ?z), 'is activated by'(?z, ?y), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
2	modulates(?othery, ?z), 'is inhibited by'(?z, ?y), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
3	binds(?othery, ?z), 'is inhibited by'(?z, ?y), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
4	'is modulated by'(?z, ?y), activates(?othery, ?z), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
5	binds(?othery, ?z), 'is binded by'(?z, ?y), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
6	'is induced by'(?z, ?y), activates(?othery, ?z), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
7	transports(?z, ?y), activates(?othery, ?z), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
8	inhibits(?othery, ?z), 'is inhibited by'(?z, ?y), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
9	metabolizes(?z, ?y), blocks(?othery, ?z), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
10	'is transported by'(?othery, ?z), transports(?z, ?y), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
11	'is blocked by'(?z, ?y), blocks(?othery, ?z), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
12	induces(?othery, ?z), 'is induced by'(?z, ?y), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
13	'is inhibited by'(?z, ?y), 'related with'(?othery, ?z), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
14	induces(?othery, ?z), transports(?z, ?y), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
15	carries(?z, ?y), blocks(?othery, ?z), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
16	'has pharmacological target'(?othery, ?z), 'is pharmacological target of'(?z, ?y), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
17	metabolizes(?z, ?y), activates(?othery, ?z), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
18	modulates(?othery, ?z), 'is pharmacological target of'(?z, ?y), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
19	'is pharmacological target of'(?z, ?y), inhibits(?othery, ?z), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
20	'is carried by'(?othery, ?z), carries(?z, ?y), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
21	carries(?z, ?y), activates(?othery, ?z), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
22	binds(?othery, ?z), 'is pharmacological target of'(?z, ?y), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
23	'is pharmacological target of'(?z, ?y), 'related with'(?othery, ?z), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
24	induces(?othery, ?z), metabolizes(?z, ?y), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
25	carries(?z, ?y), induces(?othery, ?z), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
26	'is inhibited by'(?z, ?y), blocks(?othery, ?z), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
27	binds(?othery, ?z), 'is activated by'(?z, ?y), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
28	modulates(?othery, ?z), transports(?z, ?y), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
29	modulates(?othery, ?z), 'is induced by'(?z, ?y), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)
30	binds(?othery, ?z), transports(?z, ?y), DifferentFrom (?othery, ?y) -> 'may interact with'(?othery, ?y)

Figure 1: Inference rules in DINTO: first set, rules 1-30

Figure 2 shows SWRL rules 31-59 of the first ruleset as developed in DINTO.

31) modulates(?othery, ?z), 'is modulated by'(?z, ?y), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
32) 'is metabolised by'(?othery, ?z), metabolizes(?z, ?y), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
33) 'is inhibited by'(?z, ?y), activates(?othery, ?z), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
34) binds(?othery, ?z), 'is modulated by'(?z, ?y), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
35) 'is modulated by'(?z, ?y), 'related with'(?othery, ?z), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
36) inhibits(?othery, ?z), transports(?z, ?y), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
37) 'is pharmacological target of'(?z, ?y), blocks(?othery, ?z), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
38) 'related with'(?othery, ?z), 'is activated by'(?z, ?y), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
39) binds(?othery, ?z), 'is induced by'(?z, ?y), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
40) 'related with'(?othery, ?z), transports(?z, ?y), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
41) 'is inhibited by'(?z, ?y), induces(?othery, ?z), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
42) 'is induced by'(?z, ?y), 'related with'(?othery, ?z), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
43) carries(?z, ?y), inhibits(?othery, ?z), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
44) binds(?othery, ?z), 'is blocked by'(?z, ?y), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
45) 'is pharmacological target of'(?z, ?y), activates(?othery, ?z), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
46) carries(?z, ?y), binds(?othery, ?z), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
47) blocks(?othery, ?z), 'is activated by'(?z, ?y), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
48) carries(?z, ?y), modulates(?othery, ?z), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
49) modulates(?othery, ?z), metabolizes(?z, ?y), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
50) binds(?othery, ?z), metabolizes(?z, ?y), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
51) 'is modulated by'(?z, ?y), blocks(?othery, ?z), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
52) 'is pharmacological target of'(?z, ?y), induces(?othery, ?z), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
53) inhibits(?othery, ?z), metabolizes(?z, ?y), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
54) transports(?z, ?y), blocks(?othery, ?z), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
55) carries(?z, ?y), 'related with'(?othery, ?z), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
56) 'related with'(?othery, ?z), metabolizes(?z, ?y), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
57) 'related with'(?othery, ?z), 'related with'(?z, ?y), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
58) 'is induced by'(?z, ?y), blocks(?othery, ?z), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)
59) 'related with'(?othery, ?z), 'is blocked by'(?z, ?y), **DifferentFrom** (?othery, ?y) -> 'may interact with'(?othery, ?y)

Figure 2: Inference rules in DINTO: first set, rules 31-59

2 Inferenced DDIs by rule

2.1 Before ruleset simplification

Table 1 shows the results obtained in the first analysis of the inferential process, which featured no exclusions at all.

Rule	Inferred DDIs	Rule	Inferred DDIs	Rule	Inferred DDIs
1	3,360	21	0	41	36,963
2	15	22	591	42	1,481
3	65	23	16,662	43	0
4	49	24	50,827	44	166
5	115	25	0	45	7,671
6	8	26	522	46	0
7	0	27	78	47	5,526
8	82,584	28	0	48	0
9	76	29	4	49	0
10	15,795	30	0	50	0
11	0	31	1	51	23
12	6,528	32	131,182	52	0
13	15,752	33	47	53	136,852
14	7,305	34	4	54	54
15	0	35	74	55	0
16	19,306	36	38,049	56	6,050
17	10	37	13,308	57	65,209
18	81	38	4,290	58	34
19	0	39	4	59	3,913
20	0	40	1,573	TOTAL	344,858

Table 1: Number of inferred DDIs per rule of inference.

2.2 After ruleset simplification

Some inference rules had proved to be of little consequence and were subsequently removed. Table 2 shows the results.

Rule	Inferred DDIs	Rule	Inferred DDIs
1	3,360	28	0
2	15	29	4
4	49	31	1
6	8	32	131,182
7	0	33	47
8	82,584	36	38,049
9	76	37	13,308
10	15,795	41	36,963
11	0	45	7,671
12	6,528	47	5,526
14	7,305	49	0
16	19,306	51	23
17	10	52	0
18	81	53	136,852
19	0	54	54
24	50,827	58	34
26	522	TOTAL	263,735

Table 2: Number of inferred DDIs per rule of inference.

2.3 After discarding well-known, asserted DDIs

Finally, those inferred DDIs which were already in DINTO-Graph were discarded. Table 3 presents the results after the dismissal of such DDIs.

Rule	Inferred DDIs	Rule	Inferred DDIs
1	3,287	28	0
2	15	29	3
4	49	31	1
6	8	32	127,418
7	0	33	45
8	79,220	36	36,607
9	67	37	12,732
10	15,052	41	35,200
11	0	45	7,378
12	6,138	47	5,155
14	6,744	49	0
16	18,635	51	23
17	10	52	0
18	80	53	131,797
19	0	54	53
24	49,006	58	33
26	481	TOTAL	256,851

Table 3: Some comparative figures on the number of inferred DDIs, which were not previously asserted in DINTO.

3 DDI inferences by drug families

Table 4 is the complete version of the table representing the inferential statistics arranged by drug families. It is note that it has been divided into two halves as it did not fit within a single page.

Drug family	#Drug instances	Asserted DDI rat.	#Inferred DDIs	Pct. of inf. DDIs
Anaesthetics	76	3.01	13,378	5.35%
Anti-anaemic agents	2	0	0	0%
Anti-asthmatic agents	37	12.51	9,919	3.86%
Anti-asthmatic drugs	33	12.36	8,499	3.31%
Anti-inflammatory agents	193	5.83	30,849	12.01%
Anti-inflammatory drugs	150	6.67	28,349	11.04%
NSAIDs ¹	102	5.34	17,956	6.99%
Drugs	3,020	3.38	233,764	91.01%
Anaesthetics	76	3.01	13,378	5.35%
Analgesics	146	9.05	32,494	12.65%
Angiogenesis inhibitors	22	5.23	3,981	1.55%
Angiogenesis modulating agent	14	1.71	772	0.30%
Antacids	6	6.5	0	0%
Anti-allergic agents	59	3.93	12,094	4.71%
Anti-estrogens	8	1	585	0.23%
Anti-ulcer drug	26	11.12	6,888	2.68%
Antidyskinesia agent	46	6.35	11,401	4.44%
Antiemetics	48	11.85	14,829	5.77%
Antihyperplasia drug	3	1.33	1,680	0.65%
Antiinfective agents	558	4.23	51,923	20.22%
Antimicrobial drugs	473	4.71	45,497	17.71%
Antibacterial drugs	217	5.78	23,137	9.00 %
Antiviral drugs	60	9.67	12,499	4.89 %
Antiparasitic agents	269	2.53	17,050	6.64 %
Anthelmintic drugs	37	0.68	1732	0.67 %
Antiplasmodial drugs	159	2.92	10,039	3.91 %
Antiprotozoal drugs	230	2.77	15,140	5.89 %
Ectoparasitides	2	0	555	0.22 %

¹ Acronym of Nonsteroidal anti-inflammatory drugs.

Drug family	#Drug instances	Asserted DDI rat.	#Inferred DDIs	Pct. of inf. DDIs
Antiseptic drugs	18	0.33	817	0.32 %
Antilipemic drugs	38	8.45	10,285	4.00 %
Antineoplastic agents	1,033	1.50	57,137	22.25 %
Antipyretics	33	6.67	7,319	2.85 %
Antirheumatic drugs	119	6.78	22,544	8.78 %
Antitussives	19	9.16	4,813	1.87 %
Appetite regulators	14	11.57	3,168	1.23 %
Astringents	14	0	3,168	1.23 %
Bile therapy drugs	1	0	9	0.0035 %
Bone density conservation agents	21	10.10	4,115	1.60 %
Bronchoconstrictor agents	4	0.25	348	0.14 %
Bronchodilator agents	41	9.83	10,470	4.08 %
Calcimimetics	2	6	678	0.26 %
Cardiovascular drugs	267	9.50	51,713	20.13 %
CNS ² drugs	252	11.88	63,632	24.77 %
Depigmentation drugs	15	0	2	0.00078 %
Dermatologic drugs	64	6.34	10,739	4.18 %
Diuretics	20	8.65	2,926	1.14 %
Estrogen receptor antagonists	3	23.33	1,359	0.53 %
Estrogen receptor modulators	7	28.29	3,536	1.38 %
Fibrin modulating drugs	7	9.29	1,734	0.68 %
Gastrointestinal drugs	27	4.19	4,386	1.71 %
Hematologic agents	87	10.39	11,537	4.49 %
Hormone receptor modulators	77	8.12	19,515	7.60 %
Hypoglycemic agents	41	6.34	8,129	3.16 %
Immunomodulators	79	9.92	16,686	6.50 %
Interferon inducers	1	0	621	0.24 %
Laxatives	10	0	621	0.24 %
Mydriatic agents	7	13.29	1,843	0.72 %
Neuromuscular agents	62	7.97	9,886	3.85 %
Neurotransmitter agents	548	8.65	101,000	39.32 %
Nootropic agents	3	35.67	1,385	0.54 %
Nutraceuticals	48	0.54	2,899	1.13 %
Ophthalmology drugs	31	2.94	3,779	1.47 %
Orphan drugs	5	3.4	1,554	4.49 %
Oxytocics	9	4	1,142	0.44 %
PNS ³ drugs	24	4.58	4,357	1.69 %
Photosensitizing agents	29	4.03	4,640	1.81 %
Prodrugs	105	3.88	11,309	4.40 %
Proteasome inhibitors	14	0.29	1,078	4.20 %
Protective agents	98	3.82	9,098	3.54 %
Renal agents	7	5.43	1,786	0.70 %
Reproductive control drugs	31	12.48	6,504	2.53 %
Vulneraries	7	0	53	0.02 %
Diagnostic agents	15	3.07	1,691	0.66 %

Table 4: Breakdown of the results into many different families of pharmacological entities.

²Acronym of central nervous system.

³Acronym of peripheral nervous system.