Screening of Western Drug Adulterants in Complementary Health Products by High Performance Liquid Chromatography/Diode Array Detection/Mass Spectrometry

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Gas chromatography/mass spectrometry (GC/MS) and high performance liquid chromatography/diode array detection (HPLC/DAD) are the techniques used for screening most of the common western drug adulterants in complementary health products. However, co-elution with poor baseline separation of peaks is commonly observed with complex sample matrices, thus posing a challenge for identifying any suspected drugs. Hence, we see the need to develop a high performance liquid chromatography/diode array detection/mass spectrometry (HPLC/DAD/MS) screening method based on the detection of the molecular ion, ultraviolet (UV) spectra and the retention time of each drug. This method was successfully established for 213 drugs, together with their respective limit of detection (LOD). An In-house UV library and In-house MS library, both comprising more than 200 drug substances, were also successfully built and used in the HPLC/DAD/MS screening of western drug adulterants in complementary health products.

1. Introduction

In Singapore, complementary health products generally include the Chinese proprietary medicines, traditional medicines and health supplements. These products are widely used to maintain or improve health, with public beliefs that the complementary health products are safe and have no side effects [1]. One of the greatest safety concerns of complementary health products is adulteration with undeclared pharmaceutical drugs and their analogues, in illicit attempts to evade detection [2,3,4]. It represents a problem in product quality and is one of the major causes for adverse events [5].

The more commonly used techniques for screening western drug adulterants in complementary health products are gas chromatography/mass spectrometry (GC/MS) and high performance liquid chromatography/diode array detection (HPLC/DAD) [6,7]. However, HPLC/DAD screening method commonly encountered issue of co-elution with poor baseline separation of peaks especially for complex sample matrices, thus posing a challenge for identifying any suspected drugs.

Due to its desirable sensitivity and selectivity, liquid chromatography/mass spectrometry (LC/MS) method has been applied for screening purposes too in health supplements [8,9,10]. As health supplements have complicated matrices, LC/MS would be a more suitable screening technique since it is highly selective and is capable of providing additional information about the molecular mass of the drugs. HPLC method coupled with diode array detection and electrospray ionisation mass spectrometry (HPLC/DAD/MS) could potentially eliminate false negative results and enhance the screening capability. A few reports focused on screening of a limited number of western drug adulterants by HPLC/DAD/MS [9,11]. There has not been a report on simultaneous screening of a wide range of western drug adulterants in complementary health products by HPLC/DAD/MS so far. Thus, a specific method that can simultaneously screen a wide range of western drug adulterants in complementary health products needed to be developed.

In this study, a HPLC/DAD/MS method was developed as a screening method for a wide range of western drug adulterants in complementary health products based on the detection of the molecular ion, ultraviolet (UV) spectra and the retention time of each drug in a single run. An in-house UV library and in-house MS library were also successfully built and used in the screening of western drug adulterants in complementary health products.

2. Experimental

2.1 Materials

The majority of the standard drugs (150 drugs) used were purchased from United States Pharmacopoeia (Rockville, MD, USA), British Pharmacopoeia (Teddington, Middlesex, UK) or the European Pharmacopoeia (Strasbourg, France). The remaining 63 secondary standard drugs

Table 1. HPLC/DAD/MS instrument parameters.

Instrument:	Agilent 1260 Infinity II HPLC/DAD coupled with Single Quadrupole MS 6135B
Ion source:	Electrospray Ionisation, positive and negative mode
Mass scan mode:	Full scan
Drying gas:	Nitrogen, 12 L/min at 350°C
Nebuliser gas:	Nitrogen, 35 psi
Fragmentor voltage:	70 V
Capillary voltage:	3000 V
Column:	Accucore C18, 150 mm x 2.1 mm x 2.6 µm
Oven temp:	30°C
Injection volume:	5 µL
Flow rate:	0.3 mL/min
Detection:	210, 254, 280 nm (reference 380 nm)
Mobile phase:	A : 0.1% Formic acid in H_2O B : 0.1% Formic acid in ACN
Gradient:	Time (min) A (%) B (%) 0.01 95 5 1.00 95 5 20.00 5 95 25.00 5 95 25.50 95 5 30.00 95 5

were acquired from TLC Pharmaceutical Standards Ltd. (Aurora, Ontario, Canada) or Sigma-Aldrich (St. Louis, MO, USA). All 213 standards were prepared in methanol to achieve a concentration of 1 mg/mL. They were then further diluted to 0.1 mg/mL using methanol for injection into the HPLC/DAD/MS system.

2.2 HPLC/DAD/MS screening

An Agilent 1260 series Infinity II HPLC chromatograph with diode-array detector and coupled with single quadrupole mass spectrometer detector (MSD) 6135B with electrospray ionisation (ESI) (Waldbronn, Germany) was used for the analysis. The column used was a Thermo Scientific Accucore C18, 150 mm x 2.1 mm, 2.6 µm (PA, USA). The UV spectra from 200 to 400 nm were recorded online during the chromatographic run. The mass spectra were acquired at a mass range from m/z 100 to 1000. The method conditions are listed in Table 1.

2.3 Sample preparation

The ten complementary health products selected for the study were in the form of capsules, granules, pills, powder and liquid. Capsules were opened and the contents were used for analysis. Granules and pills were ground before use. Powder and liquid samples were directly used for analysis. All the samples were thoroughly homogenised before the test. About 1 g of the homogenised sample, pre-spiked with selected western drug adulterants, was transferred to a test-tube and 10 mL of methanol was added. The mixture was sonicated in an ultrasonic bath for 15 minutes and filtered using a 0.45 µm PTFE membrane filter, which had been validated and showed no adsorption, for HPLC/DAD/MS analysis.

3. Results and Discussion

3.1 Development of UV and MS library

The UV spectra of the 213 standard drugs were obtained using DAD and compiled as an UV library using the OpenLAB CDS ChemStation Data Analysis software (Agilent Technologies). The screening of the drugs in complementary health products was carried out by library search using the same software. The UV spectra corresponding to the peaks in the unknown sample were compared with those in the library. Library matches of UV spectra were automatically calculated for each peak and a score of 1000 represented a perfect match, while a score of below 900 represented a poor match [12]. A peak identification result with a library match above 950 could be considered as identification with good certainty. For the LC/DAD library search, the retention time window was set at ± 20% and the match threshold was set at 900. For those peaks with close retention times (± 1 min) to those drug substances suggested by the In-house library and library match ≥ 900, the UV spectra of the peaks would be matched with those of the reference drug substances from the library to identify the presence of any adulterants.

The MS spectra of the 213 standard drugs were obtained using the single quadrupole mass spectrometer. The mass-to-charge ratio (m/z) of the molecular ion and retention time of the 213 drugs were compiled as a MS library using Microsoft Access. The screening of the drugs in Complementary Health Products was carried out by library search using our In-house developed program 'MS Library Search Report Generator' with retention time window set at ± 1 min and ion mass window set at ± 0.2 Da. The m/z and retention time corresponding to the peaks in the unknown sample were compared with those in the library. Library matches were automatically calculated for each peak and a score of 100 represented a perfect match. For those peaks with close retention times (± 1 min) and m/z within ± 0.2 Da to those reference drug substances suggested by the In-house LCMS library, they would be listed as suspect adulterants.

Table 2 shows the drug name, retention time, molecular ion and limit of detection (LOD) of the 213 drugs in the UV and MS library.

Co-elution of two or more compounds remains one of the major causes of errors in the HPLC/DAD screening method. Thus, the development of the in-house UV library and in-house MS library would be very useful in the HPLC/DAD/MS screening of western drug adulterants in Complementary Health Products since MS is a much more selective technique than DAD.

3.2 Screening of western drug adulterants in Complementary Health Products

To validate the HPLC/DAD/MS screening system, two positive samples (each containing one drug) and eight negative

Table 2. Retention time (RT), molecular ion and LOD of the 213 drugs in the UV and MS library.

No.	Drug Name	RT (min)	Molecular ion m/z	LOD (mg/L)	No.	Drug Name	RT (min)	Molecular ion m/z	LOD (mg/L)
1	2-(2-Ethoxyphenyl)-5-methyl-7-propyl-3H-imidazo[5, 1-f][1,2,4] triazin-4-one	12.4	313.1	5	37	Chlorothiazide (-)	3.5, 4.7	293.9 (-)	5
2	Acebutolol	8.3	337.1	10	38	Chlorpropamide	12.5	277.0	5
3	Acetazolamide	3.3, 4.1	222.9	20	39	Cimetidine	1.0, 2.2	253.1	5
4	Acetil acid	12.6	357.1	10	40	Ciprofloxacin	8.0	332.1	5
5	Acetildenafil	9.8	467.2	20	41	Clenbuterol	8.4	277.0	5
6	Acetohexamide	13.1	325.1	5	42	Clobenzorex	10.4	260.1	10
7	Acetylcysteine	1.7	164.0	50	43	Clobetasol Propionate	16.5	467.1	5
8	Albendazole	11.1	266.0	5	44	Clomipramine	12.1	315.1	5
9	Alprostadil (-)	13.0	353.1 (-)	50	45	Clorazepate	12.4	271.0	5
10	Amiloride	1.0, 2.4	230.0	20	46	Clotrimazole	12.1	277.0	5
11	Aminotadalafil	12.0	391.0	5	47	Cloxacillin	13.5	436.0	5
12	Amiodarone	15.6	646.0	5	48	Colchicine	10.4	400.1	5
13	Amlodipine	11.4	409.1	10	49	Cyclopenthiazide	13.5	380.0	5
14	Amodiaquine	1.0, 6.8	356.1	10	50	Cyproterone Acetate	16.4	417.1	5
15	Amoxicillin	1.1, 2.2	366.1	20	51	Danazol	16.7	338.2	5
16	Ampicillin	7.5	350.1	20	52	Desethylacetildenafil	9.5	439.2	20
17	Apomorphine	1.0, 7.5	268.1	5	53	Desmethylacetildenafil	9.8	453.2	20
18	Aspirin (-)	9.7	179.0 (-)	50	54	Desmethylsildenafil	10.5	461.1	5
19	Atenolol	1.0, 2.1	267.1	50	55	Desoxymethasone	12.8	377.2	5
20	Baclofen	5.6	214.0	20	56	Di-iodothyronine	10.1	525.8	5
21	Bambuterol	9.1	368.2	10	57	Diazoxide	9.7	230.9	20
22	Beclomethasone	12.2	409.1	5	58	Diflucortolone-21-Valerate	17.7	479.2	5
23	Bendroflumethiazide	13.3	422.0	5	59	Digitoxin (-)	13.9	809.3 (-)	5
24	Betaxolol	10.1	308.2	20	60	Digoxin (-)	11.1	825.3 (-)	5
25	Bezafibrate	13.8	362.1	5	61	Dimethylsildenafil	10.8	489.1	5
26	Bisoprolol	9.3	326.2	50	62	Diphenoxylate	13.3	453.2	5
27	Brompheniramine	9.2	319.0	20	63	Dipyridamole	10.4	505.3	10
28	Buclizine	15.1	433.2	5	64	Dobutamine	7.9	302.1	20
29	Bumetanide	14.1	365.0	5	65	Domperidone	9.8	426.1	5
30	Captopril	8.6	218.1	20	66	Doxazosin	10.5	452.1	5
31	Carbamazepine	11.7	237.1	5	67	Doxycycline	9.8	445.1	20
32	Carbodenafil	9.6	453.2	10	68	Droperidol	9.9	380.1	5
33	Carvedilol	11.2	407.1	5	69	Emetine	1.0, 7.6	481.2	10
34	Cefaclor	6.6, 6.9	368.0	50	70	Ergometrine	1.0, 6.8	326.1	20
35	Chlordiazepoxide	9.4	300.0	20	71	Fenbufen	14.1	255.1	5
36	Chloropretadalafil	16.0	427.0	5	72	Fenofibrate	20.0	361.1	5

No.	Drug Name	RT (min)	Molecular ion m/z	LOD (mg/L)	No.	Drug Name	RT (min)	Molecular ion m/z	LOD (mg/L)
73	Finasteride	14.0	373.2	5	109	Ketorolac Tromethamine	12.3	256.1	10
74	Fluocinolone Acetonide	12.6	453.1	10	110	Labetalol	9.6	329.2	5
75	Fluocinonide	15.2	495.1	10	111	Liothyronine	11.3	651.7	5
76	Flupenthixol/Flupentixol	12.2	435.1	5	112	Lisinopril	6.6	406.2	50
77	Flurbiprofen	15.2	245.0	5	113	Loperamide	12.6	477.2	5
78	Fluticasone Propionate	16.6	501.1	5	114	Loprazolam	10.3	465.1	5
79	Fluvastatin (-)	15.4	410.1 (-)	5	115	Lorazepam	12.4	321.0	5
80	Formoterol	8.6	345.1	5	116	Lormetazepam	13.5	335.0	5
81	Furosemide (-)	11.8	328.9 (-)	5	117	Mebendazole	11.1	296.1	5
82	Fusidic acid (-)	17.6	515.3 (-)	20	118	Medroxyprogesterone Acetate	16.9	387.2	5
83	Gendenafil	14.2	355.1	5	119	Medroxyprogesterone Base	15.4	345.2	10
84	Glibenclamide	15.7	494.1	5	120	Mefenamic acid	16.9	242.1	5
85	Gliclazide	14.3	324.1	10	121	Megestrol Acetate	16.6	385.2	5
86	Glimepiride	16.1	491.1	5	122	Megestrol Base	15.0	343.2	5
87	Glipizide	13.0	446.1	5	123	Metformin	1.0	130.1	50
88	Homosildenafil	10.7	489.2	5	124	Methimazole	1.6	115.1	20
89	Hydralazine	1.0, 1.4	161.1	100	125	Methyldopa	1.0, 1.3	212.1	20
90	Hydrochlorothiazide (-)	4.5, 5.8	295.9 (-)	5	126	Methylprednisolone	11.7	375.2	5
91	Hydroxyacetildenafil	9.7	483.2	20	127	Metoclopramide	8.0	300.1	5
92	Hydroxychloroquine	1.0, 5.4	336.1	20	128	Metolazone	11.6	366.0	5
93	Hydroxyhomosildenafil	10.5	505.2	5	129	Metoprolol	8.4	268.1	50
94	Hydroxyprogesterone 17-alpha	14.4	331.2	5	130	Mexiletine	8.6	180.1	50
95	Hydroxyprogesterone Caproate	19.9	429.2	5	131	Minocycline	6.9	458.1	20
96	Hydroxythiohomosildenafil	12.4	521.1	10	132	Mometasone Furoate	16.7	521.1	5
97	Hydroxyvardenafil	9.6	505.1	20	133	N-Desethylvardenafil	9.6	461.1	20
98	Hyoscine/Scopolamine	6.1	304.1	20	134	Naproxen	13.7	231.1	5
99	Methscopolamine	6.8	318.1	50	135	Nateglinide	15.9	318.2	10
100	Hyoscine N-Butylbromide	9.2	360.2	100	136	Nicardipine	11.5	480.1	10
101	Imidazosagatriazinone	16.1	313.1	5	137	Niclosamide (-)	17.2	324.9 (-)	5
102	Imipramine	11.3	281.2	5	138	Norgestimate	17.1, 17.4	370.2	10
103	Indapamide	12.3	366.0	5	139	Norgestrel	15.0	313.2	5
104	Indomethacin	15.7	358.1	5	140	Norneosildenafil	16.6	460.1	5
105	Isoconazole	13.4	416.9	5	141	Nortriptyline	11.5	264.1	5
106	Itraconazole	16.6	705.2	5	142	Noscapine	9.6	414.1	5
107	Ketoconazole	11.3	531.1	5	143	Ofloxacin	1.1, 7.9	362.1	5
108	Ketoprofen	13.6	255.1	5	144	Omeprazole	9.2	346.1	10

No.	Drug Name	RT (min)	Molecular ion m/z	LOD (mg/L)	No.	Drug Name	RT (min)	Molecular ion m/z	LOD (mg/L)
145	Ondansetron	9.1	294.1	5	181	Sildenafil Related Compound	10.1	463.1	5
146	Oseltamivir	9.6	313.2	10	182	Simvastatin	19.1	441.2	20
147	Oxazepam	12.2	287.0	5	183	Spironolactone	14.7	341.2	5
148	Oxprenolol	9.2	266.1	10	184	Stanozolol	13.1	329.2	10
149	Oxymetholone	17.7	333.2	10	185	Sulfadiazine	3.3, 4.2	251.0	5
150	Paroxetine	11.2	330.1	10	186	Sulfadoxine	9.9	311.0	20
151	Penicillin G (-)	11.7	333.0 (-)	10	187	Sulindac	12.6	357.0	5
152	Penicillin V (-)	12.4	349.0 (-)	10	188	Tadalafil	12.8	390.1	5
153	Perphenazine	11.3	404.1	10	189	Telmisartan	11.6	515.2	5
154	Phenformin	4.0	206.1	20	190	Terazosin	8.4	388.2	5
155	Phenoxybenzamine	13.6	304.1	50	191	Terbutaline	1.0, 1.9	226.1	50
156	Phentolamine	9.6	282.1	5	192	Terfenadine	13.5	472.3	5
157	Pholcodine	1.0, 1.3	399.2	50	193	Tetracycline	8.2	445.1	20
158	Piperiacetildenafil	10.3	438.2	5	194	Theophylline	3.7, 4.2	181.0	5
159	Piroxicam	12.1	332.0	10	195	Thiodimethylsildenafil	12.7	505.1	5
160	Pravastatin (-)	11.5	423.1 (-)	20	196	Thiohomosildenafil	12.6	505.1	10
161	Prazosin	8.9	384.2	10	197	Thiosildenafil	12.5	491.1	20
162	Primidone	8.5	219.1	5	198	Thyroxine	12.1	777.6	5
163	Probenecid (-)	14.3	284.0 (-)	5	199	Tiratricol (-)	15.2	576.6 (-)	20
164	Proguanil	10.0	254.1	10	200	Tolazamide	13.4	312.1	5
165	Propafenone	11.3	342.2	5	201	Tolbutamide	13.2	271.1	5
166	Propantheline	11.9	368.2	20	202	Torsemide	10.3	349.1	5
167	Propranolol	10.1	260.1	5	203	Tranylcypromine	3.8	134.1	50
168	Propylthiouracil	6.5, 6.6	171.1	5	204	Trazodone	9.8	372.1	5
169	Pseudovardenafil	13.8	460.1	5	205	Triamcinolone Acetonide	12.4	435.1	10
170	Pyrazole N-Desmethyl Sildenafil	9.6	461.2	20	206	Triamcinolone	9.8	395.2	5
171	Ranitidine	1.0, 2.5	315.1	20	207	Triamterene	7.5	254.1	5
172	Repaglinide	13.0	453.2	10	208	Triprolidine	9.3	279.1	10
173	Reserpine	12.1	609.2	5	209	Usnic acid	19.5	345.0	50
174	Rosiglitazone	8.9	358.1	10	210	Vardenafil	9.7	489.2	5
175	Salbutamol	1.0, 1.9	240.1	10	211	Warfarin	14.6	309.1	5
176	Salicylic acid (-)	10.1	137.0 (-)	5	212	Xanthoanthrafil/ Benzamildenafil	13.0	390.1	10
177	Sildenafil Amide	10.0	213.1	5	213	Yohimbine	9.1	355.2	5
178	Sildenafil Amine	4.0, 4.3	183.1	10	(-): Negative charged drug, deprotonated form				
179	Sildenafil	10.6	475.1	10					
180	Sildenafil Coupled	12.3	331.1	5					

Table 3. Summary of the drugs detected and the concentrations spiked in the ten complementary health products.

Product	Dosage form	Drug name	Spiked Concentration (mg/L)	RT (min)	Molecular ion m/z	LC/DAD/MS Screening	
						Detection by	
						DAD	MS
1	Capsule	Furosemide	NA (positive sample)	11.9	328.9 (-)	Detected	Detected
2	Capsule	Salicylic acid	NA (positive sample)	10.2	137.0 (-)	Detected	Detected
3	Capsule	Methyldopa	50	1.1, 1.4	212.0	Detected	Detected
		Ciprofloxacin	10	8.1	332.1	Detected	Detected
		Simvastatin	100	19.1	441.2	Detected	Detected
4	Capsule	Clobenzorex	100	10.5	260.1	Detected	Detected
		Piroxicam	20	12.2	332.0	Not Detected	Detected
5	Powder	Naproxen	20	13.9	231.0	Detected	Detected
		Fluticasone Propionate	10	16.9	501.1	Detected	Detected
6	Liquid	-	NA (negative sample)	NA	NA	No drug detected	No drug detected
7	Capsule	Desmethylsildenafil	10	10.8	461.1	Detected	Detected
		Hydroxyhomosildenafil	10	10.8	505.1	Not Detected	Detected
8	Powder	Metformin	100	1.2	130.1	Detected	Detected
		Theophylline	15	4.0, 4.5	181.1	Detected	Detected
		Medroxyprogesterone	20	15.7	345.2	Detected	Detected
9	Granule	-	NA (negative sample)	NA	NA	No drug detected	No drug detected
10	Pill	Yohimbine	10	9.3	355.2	Detected	Detected
		Indomethacin	10	16.0	358.1	Detected	Detected
NA: Not applicable							

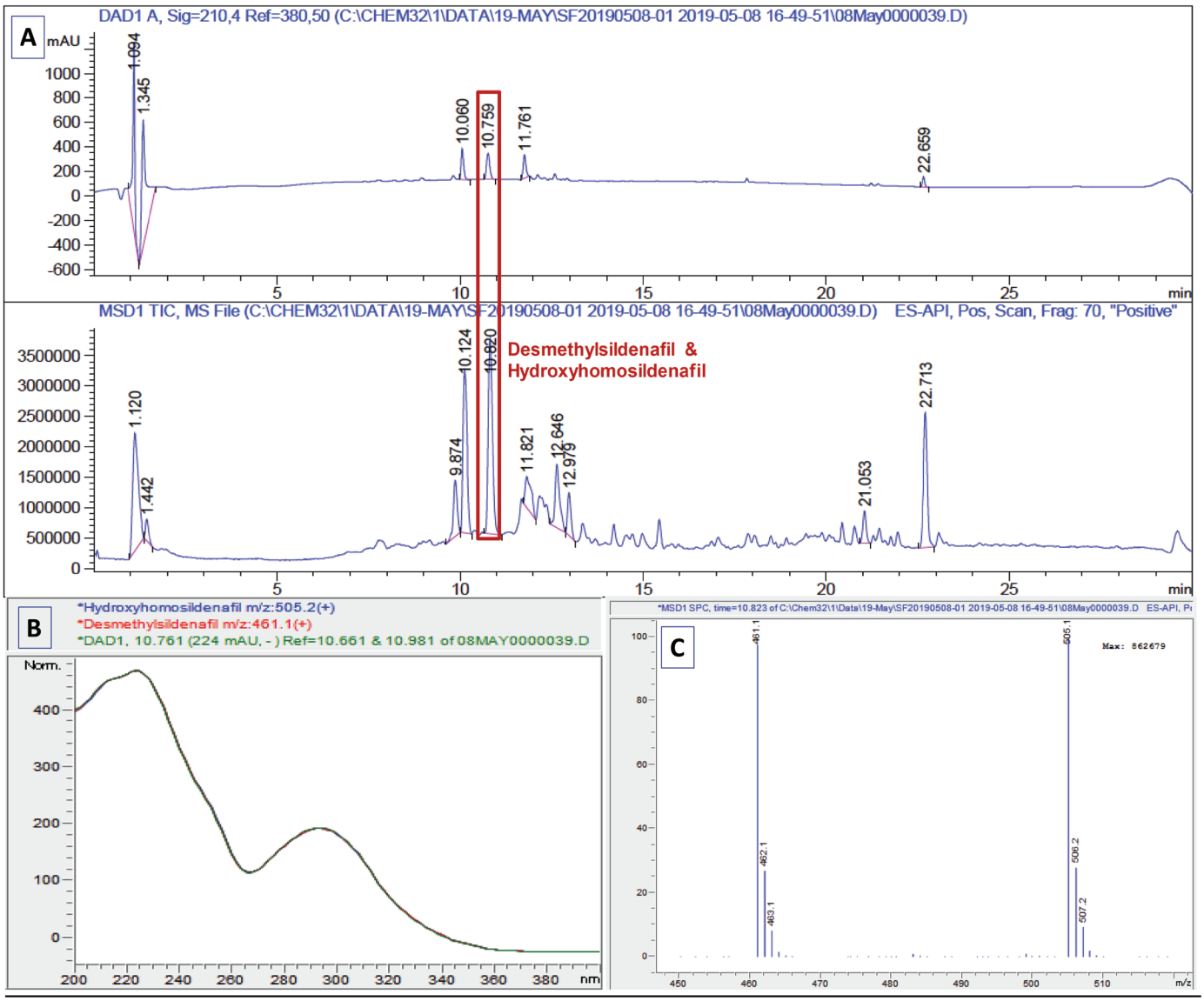
complementary health product sample matrices were selected. A total of fourteen drugs were spiked into the eight negative complementary health product sample matrices as unknowns. Table 3 showed the list of drugs that were detected in the positive samples (Product 1 and 2), and the list of drugs with their spiked concentrations in the negative samples (Product 3-5, 7-8 and 10). There were two negative samples without any drugs being spiked in (Product 6 and 9). All the ten samples were then analysed using the HPLC/DAD/MS screening system and the results were as shown in Table 3. The LC/DAD library search reports were able to successfully detect and identify fourteen out of the sixteen drugs with a library match score of more than 990, indicating a good match of UV spectra with those drugs in the UV library. Two of the drugs, namely Piroxicam in Product 4 and Hydroxyhomosildenafil in Product 7, were not detected by the LC/DAD library search report due to co-elution with other peaks at the same retention time. However, when MS technique was used in the screening, Piroxicam in Product 4 and Hydroxyhomosildenafil in Product 7 were successfully detected and identified in the LC/MS library search reports with a perfect score of 100.

For illustration, two drugs namely, Desmethylsildenafil and Hydroxyhomosildenafil with close retention times at about 10.8 min as shown in Figure 1A and identical UV spectra as shown in Figure 1B, were spiked at 10 mg/L into Product 7. The LC/DAD library search report was not able to identify Hydroxyhomosildenafil as shown in Figure 1D. The presence of m/z 461.1 in Figure 1C, represents the molecular ion $[M + H]^+$ of Desmethylsildenafil, while the ion at m/z 505.1 in Figure 1C corresponds to the molecular ion $[M + H]^+$ of Hydroxyhomosildenafil. Since both molecular ions at m/z 461.1 and 501.1 were observed in the MS spectra, this indicated that both drugs were present in Product 7. The LC/MS library search report was able to correctly identify Desmethylsildenafil and Hydroxyhomosildenafil with a good match quality as shown in Figure 1E, even though these two drugs co-eluted at the same retention time with identical UV spectra. The HPLC/DAD/MS screening method proved to be successful in the identification of all sixteen drugs in the ten samples during the study.

The limit of detection (LOD) was established as the lowest concentration at which a signal-to-noise ratio (S/N) of at least 3 was obtained for UV detection. The limit of detection (LOD) of 213 drugs were determined to be between 5 and 100 mg/L as shown in Table 2. 121 drugs had the lowest LOD of 5 mg/L. Hydralazine and Hyoscine N-Butylbromide had the highest LOD of 100 mg/L. Most of the LOD of the 213 drugs (92%) fall within the range of 5 – 20 mg/L, which is considered a reasonable limit for adulterant screening.

Due to the complexity of the matrices in complementary health products, and the co-elution of matrix and drug compounds, the UV spectra of the drugs are not be able to match the UV spectra of the drugs in the UV screening library, resulting in false negative results. It is very important therefore to use a highly selective LC/MS screening technique based on the detection of the molecular ion to complement the DAD technique, and hence avoiding false negative results.

A good data processing software programme is also required for the screening of western drug adulterants in complementary health products to conduct auto-library searches against the in-house UV and MS screening libraries. The OpenLAB CDS ChemStation Data Analysis software can do auto-library search against the UV library with retention time included in the matching, however such auto-library search function is not available for the MS library. It would be ideal to have a powerful



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Meas. RetTime [min]	Library RetTime [min]	CalTbl RetTime [min]	Sig	Area %	Purity Factor	#	Match	Name
10.060	11.148	-	1	2.51642e-3	969 u	1	922	Paroxetine HCl m/z:330.1(+)
10.060	9.109	-	1	2.51642e-3	-	1	944	? Bambuterol HCl m/z:368.2(+)
10.060	9.109	-	1	2.51642e-3	969 d	1	946	Bambuterol HCl m/z:368.2(+)
10.060	11.148	-	1	2.51642e-3	-	1	924	? Paroxetine HCl m/z:330.1(+)
10.759	10.486	-	1	2.89711e-3	984 u	1	1000	Desmethylsildenafil m/z:461.1(+)
10.759	10.583	-	1	2.89711e-3	-	1	1000	? Sildenafil Citrate m/z:475.1(+)
10.759	10.583	-	1	2.89711e-3	984 d	1	997	Sildenafil Citrate m/z:475.1(+)
10.759	10.486	-	1	2.89711e-3	-	1	997	? Desmethylsildenafil m/z:461.1(+)

E

MS Library Search

Library: C:\MS Library Search Report Generator\LCMS18 Library.accdb
RT window: 1 min
Ion mass window: 0.2
Threshold: 1

Peak RT	Compound Name	Compound RT	Molecular Weight	Match Quality	Mode
10.820	Desmethylsildenafil	10.566	460.6	100	Positive
10.820	Hydroxyhomosildenafil	10.575	504.6	100	Positive

Figure 1. Suspect peak detected from an adulterated complementary health product (A) and its UV spectra (B) and mass spectra (C) and UV library matched to Desmethylsildenafil (D) and MS library matched to Desmethylsildenafil and Hydroxyhomosildenafil (E).

data processing software suite that could generate the UV and MS library search results together in the same report, which could greatly ease data processing and interpretation.

4. Conclusion

The newly developed HPLC/DAD/MS screening method was successfully established for 213 drugs, together with their respective limit of detection (LOD) in complementary health product matrices. The study demonstrated the application of an in-house UV and MS library for effective screening and identification of 213 drugs

without the need of standards for each analysis.

5. References

1. S.R.B.M. Eussen, H. Verhagen, O.H. Klungel, J. Garssen, H.van Loveren, H J.van Kranen, C.J.M. Rompelberg, Eur. J. Pharmacol. 668 (2011) S2.
2. E. Ernst, J. Intern. Med. 252 (2002) 107.
3. T. Rocha, J.S. Amaral, M.B.P.P. Oliveira, Compr. Rev. Food Sci. Food Saf. 15 (2016) 43.
4. J. Calahan, D. Howard, A.J. Almalki, M.P. Gupta, A.I. Calderon, Planta Med. 82 (2016) 505.
5. P. A. Chyka, Am. J. Med., 2000, 109, 122–130.
6. 12. S.H. Kim, J. Lee, T. Yoon, J. Choi, D. Choi, D. Kim, S.W. Kwon, Biomed. Chromatogr. 23 (2009) 1259.
7. S.Y. Liu, S.O. Woo, H.L. Koh, J. Pharm. Biomed. Anal. 24 (2001) 983.
8. J. Wang, B. Chen, S. Yao, Food Addit. Contam. A 25 (2008) 822.
9. X. Zhu, S. Xiao, B.O. Chen, F. Zhang, S. Yao, Z. Wan, D. Yang, H. Han, J Chromat. A 1066 (2005) 89.
10. S.R. Gratz, C.L. Flurer, K.A. Wolnik, J Pharm Biomed Anal. 36 (2004) 525.
11. Z. Huang, S. Xiao, D. Luo, B. Chen, S. Yao, J Chromat Sci, 46 (2008) 707.
12. L. Huber, S. George, Diode Array Detection in HPLC, Marcel Dekker, New York, 1993.