Drug Dosage and Complementary Medicines

CONTENTS

Commonly used medicines

Drug	Dose		Times daily	Notes
ACYCLOVIR				
Herpes simplex virus				
Oral	< 2 years	100mg	4	For prophylaxis
	> 2 years	200mg	4	
	< 2 years	200mg	5	For mild mucocutaneous
	> 2 years	400mg	5	HSV
IV	250mg/m^2		3	For more serious infection or if patient cannot tolerate oral medication
Varicella zoster virus				
Oral	< 2 years	200mg	4	For prophylaxis
	> 2 years	400mg	4	For prophylaxis
	< 2 years	200mg	4	For patients with mild
	2-5 years	400mg	4	chickenpox who received
	6-12years	600mg	4	ZIG within 48 hours of
	>12 years	800mg	4	exposure or who are VZV IgG+ve
	< 2 years	200mg	4	For patients with mild
	2-5 years	400mg	4	shingles
	6-12years	600mg	4	
	>12 years	800mg	4	
IV	500mg/m^2		3	For VZV in an IgG-ve patient or any patient who has more severe VZV infection. Give for 5 days then oral treatment dose for 5 days.
Preparations:	Tablets	200mg, 400mg		
	Injection	250mg		
ADRENALINE	Injection (SC/IM)			
ALLOPURINOL				
Oral	100mg/m^2		3	Hyperuricaemia due to tumour lysis syndrome.
Preparations:	Tablets	100mg		
	iV	If available		

Drug	Dose	Times daily	Notes

AMIKACIN

IV	<1year	7.5mg/kg/ dose	Q8h	Monitor levels
IV		20mg/kg	once daily	
		600mg/m2 (max 1.5g)	Q8h	Monitor levels
Preparations:	Injection	500mg/2mL		

AMITRIPTYLINE

Oral	0.5 –1mg/kg/day (adult: 25 – 50mg)	At night	This is low dose for nerve pain
Preparations:	Tablets 10mg, 25mg, 50mg		

AMOXICILLIN

Oral/IV	10 – 25mg/kg (adult 0.25-1g)	3	Usual
IV	50mg/kg (max adult dose 2g)	Q6h	Severe infection
Preparations:	Capsules 250mg, 500mg Liquid 125mg/5mL, 250mg/5mL Injection 250mg, 500mg, 1gm		

AMOXICILLIN and CLAVULINIC ACID (AUGMENTIN®)

Dose as for amoxicillin

Preparations:	Tablet	500mg
	Syrup	125mg/5ml, 250mg/ml
	Injection	600mg, 1.2gm

AMPHOTERICIN B (non-encapsulated)

Give a test dose IV over 1-2 hours to exclude allergy. Infuse in 40ml of 5% glucose. For child < 10kg give 0.1 mg/kg up to a maximum of 1 mg, for older children give 1mg Give once daily with 5% dextrose over 6 hours, with no additives.

Then Day 1	0.3mg/kg IV
Day 2	0.6mg/kg IV
Day 3	1mg/kg IV
Day 4	Continue 1mg/kg
Preparations:	Injection 50mg

Amphotericin frequently causes rigors and pyrexias; therefore, prospectively premedicate with phenergan and hydrocortisone. Amphotericin almost invariably causes reduced GFR, therefore stop if creatinine >1.5 times above upper limit of normal and use liposomal amphotericin.

Non-encapsulated amphotericin B always causes potassium loss through kidneys. Start supplemental potassium as soon as amphotericin is started ie. do not wait for the potassium level to drop. A potassium-sparing diuretic such as amiloride may be very useful in complementing potassium replacement:

- amiloride may cause hyponatraemia
- watch potassium levels very carefully (initially 2 x daily) when using potassium supplements and amiloride together
- NEVER use potassium supplements and amiloride together when renal losses of potassium are *not* excessive – it can cause serious hyperkalaemia.

Consider use of liposomal amphotericin preparation (if available) if potassium level is difficult to support with above measures.

BENZTROPINE

Oral	0.02-0.06mg/kg (adult: 1-3mg)	1-2	For drug induced extra-pyramidal symptoms Has a cumulative action - continued observation of the patient is necessary
Intravenous	0.02-0.1mg/kg (max 2mg)	single dose	Followed if necessary by oral treatment
Preparations:	Tablets 2mg Injection 1mg/1ml		

BENZYLPENICILLIN (Penicillin G)

IV	30mg/kg	Q6h	Usual
	60mg/kg	Q6h	Severe infection
Preparations:	Injection 600mg		

BISACODYL

Oral/Rectal	>2.5 month	2.5mg	1	Stimulant laxative.
	1-5 yrs	5-10mg	1	Doses and frequency can
	> 5 yrs	10-20mg	1	be increased.
	Oral acts in 12hr (give at night),			
	Rectal acts in 20-60min (use in the morning).			
Preparations:	Tablets 5mg Suppositories 5mg, 10mg			

CALCITRIOL

Oral	0.25mcg/day	1	Hypocalcaemia
Preparations	Capsule 0.25mcg Liquid 1mcg/mL		

CARBAMAZEPINE

Oral	1mg/kg (adult: 200-800mg bd)	2	For nerve pain - increase to maintenance dose gradually.
Preparations:	Liquid 100mg/5ml Tablets 200mg, 400mg		

CEFTAZIDIME

IV	50mg/kg/dose (max dose 2g)	Q8h	
Preparations:	Injection 500mg. 1gm, 2gm		

CEFTRIAXONE

IV	80mg/kg (max 2g)	Q24H	
Preparations:	Injection 250mg, 500mg, 1gm, 2gm		

CIPROFLOXACIN

Oral	5-10mg/kg (adult 250-500mg)	2	Excellent oral bioavailability
IV	4-7mg/kg (adult 200-400mg)	Q12h	Round to vial size if possible
Preparations:	Tablets 250mg, 500mg, 750mg Injection 200mg		

CLARITHROMYCIN

Oral	7.5 – 15mg/kg	2	Beware interaction with vincristine
IV	7.5mg/kg (max 500mg)	Q12h	
Preparations:	Tablets 250mg Suspension 125mg/5mls Injection 500mg		

CODEINE PHOSPHATE

Oral	0.5-1mg/kg (adult max 240mg/day)	4-6	For analgesic effect
	0.25-0.5mg/kg/dose	4-6	For anti-diarrhoea, antitussive effect
Preparations:	Linctus 15mg/5ml Tablets 15mg, 30mg		

COLOXYL DROPS® (Poloxamer)

Oral	< 6 months	10 drops	3
	6-18 months	15 drops	3
	$1^1/_2$ – 3 yr	25 drops	3
Preparations:	Oral Drops 10% 30mL		

CO-TRIMOXAZOLE (trimethoprim-sulphamethoxazole)

Cotrimoxazole Liquid (240mg/mL) Dose - Twice Daily on Saturday and Sunday			
Weight of Patient (kg)	**Suspension 240mg/5ml**	**Dose of combined cotrimoxazole (mg)**	**Dose of trimethoprim component (mg)**
3 to 3.9	**1mL**	48	8
4 to 5.5	**1.5mL**	72	12
5.6 to 7	**2mL**	96	16
7.1 to 8.8	**2.5mL**	120	20
8.9 to 10.4	**3mL**	144	24
10.5 to 12	**3.5mL**	168	28
12.1 to 13.6	**4mL**	192	32
13.7 to 15.2	**4.5mL**	216	36
15.3 to 16.8	**5mL**	240	40
16.9 to 18.4	**5.5mL**	264	44
18.5 to 20	**6mL**	288	48
20.1 to 21.6	**6.5mL**	312	52
21.7 to 23.2	**7mL**	336	56
23.3 to 24.8	**7.5mL**	360	60
24.9 to 26.4	**8mL**	384	64
26.5 to 28	**8.5mL**	408	68
28.1 to 29.6	**9mL**	432	72
29.7 to 31.2	**9.5mL**	456	76
31.3 to 32.8	**10mL**	480	80
Cotrimoxazole tablet (480mg) Dose - Twice Daily on Saturday and Sunday			
Weight of Patient (kg)	**480mg tablet**	**Dose of combined cotrimoxazole (mg)**	**Dose of trimethoprim component (mg)**
15 to 22.5	**½ tablet**	240	40
22.6 to 37.5	**1 tablet**	480	80
37.6 to 52.5	**1 ½ tablets**	720	120
> 52.6	**2 tablets**	960	160

IV	30mg/kg		Q6h	For established PCP. Give IV for 7 days, then change to oral for 7 days
Preparations	Syrup	240mg/5mL		
	Tablet	480mg		
	Injection	480mg		

CYCLIZINE

Oral, IV	0.5mg/kg		3	
OR	< 1 year	0.5mg/kg	3	Particularly for emesis of raised intracranial pressure
	1- 4 yr	12.5mg	3	
	6- 12 yr	25mg	3	
	> 12 yr	50mg	3	
Subcutaneous	Total daily dose as above			
Preparations:	Tablets	50mg		
	Injection	50mg/ml - can be given orally		

CAUTION: Cyclizine when given concurrently with morphine can cause over sedation

DEXAMETHASONE

Oral / IV	< 3 yr	2mg	3-4	**Antiemetic**
	3-5 yr	4mg	3-4	Maximum of 12 doses per chemotherapy course
	5-10 yr	6mg	3-4	
	> 10 yr	8mg	3-4	
or	0.1 - 0.25mg/kg/dose		3-4	Also reduces tumour swelling. Use minimum dose for effect; short course and taper dose
Preparations:	Tablets	1mg, 4mg		
	Liquid	1mg/ml		
	Injections	4mg/ml - can be given orally.		

DIAZEPAM

Oral	0.04-0.2mg/kg		3	Anxiolytic/Anti-spasmodic
Rectal tubes	1-3 yr	5mg	single dose	Anticonvulsant. Repeat if needed
	4-12 yr	10mg		
Intravenous	0.25mg/kg		single dose	Anticonvulsant. Slow intravenous over 3 min, repeat if needed in 5 min
	0.1mg/kg/hr		continuous	Starting dose after bolus
Preparations:	Tablets	2mg, 5mg, 10mg,		
	Rectal tubes	5mg, 10mg		
	Injection	10mg/2ml		

DICLOFENAC

Oral/Rectal	1-3mg/kg (max adult =150mg/24h)	2-3	Slow release preparations given once or twice daily.
Preparations:	Tablets	25mg, 50mg, 50mg dispersible	
	Slow release	75mg SR, 100mg SR	
	Suppositories	12.5mg, 25mg, 50mg, 100mg	

Diclofenac may temporarily inhibit platelet aggregation. Patients with defects of haemostasis should be carefully monitored.
Diclofenac should be used cautiously in children with low platelet counts, as bleeding may be enhanced.

As fluid retention and oedema have been reported in association with NSAID therapy, particular caution is called for in patients with impaired cardiac or renal function, history of hypertension, patients receiving concomitant treatment with diuretics or medicinal products that can significantly impact renal function

DICLOXACILLIN

Oral/IV	10mg/kg	4	Usual
	25-50mg/kg (max 2g)	4	Severe infection
Preparations:	Capsules	250mg, 500mg	
	Syrup	125mg/5mL, 250mg/5mL	
	Injection	500mg, 1gm	

DOCUSATE SODIUM (Coloxyl)

Oral	< 3 years	see coloxyl drops		Stimulant/softener. Large initial doses and reduce; Acts in 1-2 days.
	3 – 6 yrs	50mg	1	
	6-12 yrs	120mg	1	
Preparations	Tablets	50mg, 120mg		

DOMPERIDONE

Oral	0.2-0.4mg/kg	4	
Preparations:	Tablets	10mg	

ERYTHROMYCIN

If planning to use IV, preferably use clarithromycin which is more expensive than erythromycin but erythromycin IV is more emetogenic than most chemotherapy!

Oral	12.5mg/kg	4	Beware interaction with vincristine
Preparations:	Tablets	400mg	
	Syrup	200mg/5mL, 400mg/5mL	

FLUCLOXACILLIN

Oral/IV	10mg/kg	4	Use dicloxacillin if concerns about liver problems.
	25mg/kg (max 2g)	4 (severe)	
Preparations:	Capsules	250, 500mg	
	Suspension	125mg/5mL, 250mg/5mL	
	Injection	250mg, 500mg, 1gm	

FLUCONAZOLE

Oral/IV	3mg/kg (max 150mg)	1	Antifungal prophylaxis
	3 - 6mg/kg	od for 7-14 days	For mucosal candidiasis. Can go up to 12mg/kg for invasive candidiasis
Preparations:	Capsules	50mg, 150mg, 200mg	
	Suspension	50mg/5ml	

	Injection	2mg/ml	

GENTAMICIN

IV	7.5mg/kg	Once daily	Infuse over 30 minutes Monitoring required.
	Take peak level 30 minutes after end of 30 minute infusion, trough level 6 – 14 hrs after infusion		
Preparations	Injection	80mg/2mL	

HALOPERIDOL

Oral/SC	0.01-0.1mg/kg	3	Lower doses required for nausea. Avoid high doses or prolonged courses because of extra-pyramidal side-effects
Preparations:	Tablets	0.5mg, 1.5mg, 5mg	
	Liquid	2mg/ml	
	Injection	5mg/ml	

HYOSCINE BUTYLBROMIDE (Buscopan®)

Oral/IM/IV	0.5mg/kg (max 40mg)	3 – 4	Antispasmodic
Preparations:	Injection	20mg/ml (can be given orally)	
	Tablet	10mg	

IBUPROFEN

Oral	5-10mg/kg (adult:150-600mg)	3-4	Beware in patients at risk of renal dysfunction.
Preparations:	Tablets	200mg, 400mg, 600mg	
	Slow Release	800mg SR	
	Suspension	100mg/5ml	

Can interfere with platelet function and should be used cautiously in children with low platelet counts, as bleeding may be enhanced.

Avoid use in patients with pre-existing illnesses that may contribute to development of renal failure. Use with caution in patients with asthma

LACTULOSE

Oral	0.5-1ml/kg	1-2	Osmotic laxative. Starting dose, adjust according to response; acts over 24 hr
Preparations:	Solution	3.5g/5ml	

LEVOMEPROMAZINE - Nozinan®

Oral/IV	0.25 - 1mg/kg	3-6	Sedative and anti-emetic.
	In adults much lower doses (5mg/24hrs) have been used for anti-emesis alone. Beware of phenothiazine-like side-effects.		

IV/SC	100mcg/kg/day	Continuous infusion	Anti-emetic.
	Make up to 50ml with NaCl 0.9%, start infusion at 2ml/hr. Titrate to effect against nausea and vomiting and degree of drowsiness by ↑ or ↓ by 0.25ml /hr every six hours. Decrease as above before stopping.		
IV/SC	0.5 - 3mg/kg/24hr	Continuous infusion	Palliative care. Can be mixed with morphine
Preparations:	Tablets 25mg, 100mg Injection 25mg/ml		

LOPERAMIDE

Oral	0-4 yr		Not recommended in <4yr due to risk of respiratory depression.
	>4 yr 0.05–0.1mg/kg (max 2mg)	2 - 3	
Preparations:	Capsules 2mg		

LORAZEPAM

Oral	0.025-0.05mg (max = 2mg)	3-4	For use with other anti-emetics. Start with low dose to avoid hallucinations
Preparations:	Tablets 1mg, 2.5mg		

MEROPENEM

IV	20 – 40mg/kg (adult dose 1g-2g)	Q8h
Preparations:	INJECTION 500mg**,** 1gm	

METOCLOPRAMIDE (MAXALON)

Oral/IV	0.12mg/kg (adult 10mg)	3-4	Anti-emetic
Oral	0.3 - 0.5mg/kg	3	For emesis with chemo
Intravenous	up to 0.5mg/kg/dose as intravenous bolus	3	Check with consultant before using higher doses; dystonic reactions can occur at any dose -reverse with benztroprine

Preparations:	Tablet	10mg
	Syrup	5mg/5mL
	Injection	10mg

METRONIDAZOLE

Oral/IV	7.5mg/kg	3	
Preparations:	Tablets	200mg, 400mg	
	Solution	200mg/5mL	
	Injection	500mg/100ml	

MICROLAX ENEMA (sodium citrate)

Rectal	< 12 months	1.25ml	)	
	1 – 2 years	2.5ml	) 1	Acts in 15-30 minutes.
	> 2 years	5ml	)	
Preparations	5ml disposable pack			

MIDAZOLAM

Oral	0.5mg/kg (max 15mg)	30 minutes prior to procedure	Sedation
IV/IM	0.1 – 0.2mg/kg (max 0.5mg/kg	Once	For anxiolysis. Gives better control than diazepam.
Subcutaneous	0.02 - 0.1mg/kg/hr	Continuous infusion	For palliation. Can be mixed with morphine.

Preparations:	Oral or intranasal	Use IV 5mg/ml preparation Intranasal : 0.2-0.4 mg/kg (max 10 mg) Administration technique is important. Drop dose into alternating nostrils over 15 secs. Absorption is rapid; maximum effect in 10 mins and duration up to 2 hrs. May be irritating and should only be used if a rapid effect is required.
	Injection	1mg/ml, 5mg/ml

Drug	Dose	Times daily	Notes
MORPHINE SULPHATE			
Oral	Starting dose < 6 months 0.1mg/kg > 6 months 0.2mg/kg (limit 10mg/dose)	Q3-4h prn	Acute Pain
	For dosing in chronic pain and use of sustained release formulations refer Palliative Care Guideline		
IM	0.15 – 0.2mg/kg	Q3-4h prn	Avoid if possible
IV infusion			
SC	0.2mg/kg	q4-6h	Starting dose
IV increments	0.01-0.02mg/kg	until comfortable	RR ≥ 12 (>10yrs)
Preparations:	Mixture 1mg/mL, 5mg/mL, 10mg/mL Sevredol 10mg,20mg - Fast release tablet MST 10mg,30mg,60mg,100mg,200mg Sustained release tablet Kapanol 10mg,20mg,50mg,100mg Sustained release capsule M-Eslon 10mg,30mg,60mg,100mg,200mg Sustained release tablet		
NYSTATIN			
Oral	100 000u/ml	4	Prophylaxis
	500 000u	4	Treatment
Topical	100 000u/g	2	Treatment
Preparations	Capsule 500 000u Topical 100 000u/g - Cream or ointment Oral drops 100 000u/ml - swish and swallow after eating or drinking		
OMEPRAZOLE			
Oral	0.4-0.8mg/kg (adult 20-40mg)	1	Higher doses may be given bd. Ablates
Injection:	0.5mg/kg initially – 2mg/kg(max)	1	itraconazole absorption.
Preparations:	Capsules 10mg, 20mg, 40mg – can open and sprinkle on food Syrup 2mg/mL Injection 40mg		
ONDANSETRON – see Symptom Care Chapter (Prevention and treatment of nausea and vomiting)			
Oral/IV	0.15mg/kg (max 8mg) or <0.3m^2 0.3-0.6m^2 0.6-1.2m^2 >1.2m^2	Q6-8h prn 1mg 2mg 4mg 8mg	
Preparations:	Wafers 4mg, 8mg Tablets 4mg, 8mg Injection 4mg, 8mg		

Drug	Dose	Times daily	Notes
PARACETAMOL			
Oral	15mg/kg	Q4-6h	Maximum 90mg/kg/day
Preparations	Suspension 120mg/5mL, 250mg/5mL Tablet 500mg, 500mg dispersible		
PARAFFIN			
Oral	1ml/kg	1	Maximum 45mL
Preparation	Liquid only		
PARALDEHYDE			
Rectal	0.3ml/kg (max 10ml)	Mix with equal volume of arachis or olive oil; insert immediately if plastic syringe used; repeat 1-2 hourly if needed.	
Preparations:	Injection 5ml		
PHENOBARBITONE			
IV/SC	15mg/kg	single dose	Slow injection over 5 min.
Subcutaneous	0.5mg/kg/hr	continuous	For palliation, increase as needed, use separate infusion
Preparations:	Injection 20mg/0.5ml, 200mg/ml Tablet 15mg, 30mg		
PIPERACILLIN			
PROCHLORPERAZINE			
Oral/Rectal	0.1- 0.25mg/kg	3 - 4	For palliation. Not suitable for subcut. infusion as it is a skin irritant
IV Avoid if possible due to CVS effects	0.1–0.2mg/kg	3 - 4	
Preparations:	Tablets 5mg, 25mg Injection 12.5mg/ml		
PROMETHAZINE			
Oral / IV	0.2-0.5mg/kg (adult 10-25mg)	3-4	Anti-histamine, anti-emetic
	0.5-1.5mg/kg (adult:25-100mg)	3-4 prn	Sedative
Preparations:	Tablets 10mg, 25mg Liquid 5mg/5ml Injection 25mg/ml		
PROPANTHELINE			
Oral	0.3mg – 0.6mg/kg (max: 2mg/kg/day)	3-4	Antispasmodic, anticholinergic
Preparations:	Tablets 15mg		

Drug	Dose	Times daily	Notes
RANITIDINE			
Oral	2-4mg/kg (max daily = 300mg)	2	
IV	1mg/kg	3	
Preparations:	Tablet 150mg, 300mg Liquid 150mg/10ml Injection 50mg/2ml		
SENNA			
Oral	< 2 yr ½ - 1 tablet 3-10 yr 1-2 tablets > 10 yr 2-4 tablets	1 1-2 1-2	Stimulant. Acts in 8-12 hrs
Preparations:	Tablets 7.5mg		
SUCRALFATE			
Oral	0 – 2yrs 0.25gm 3-12 yrs 0.5gm > 12yrs 1gm	4 4 4	Mucositis
Preparations	Tablet 1gm		
TIMENTIN (Ticarcillin/Clavulanate)			
IV	300mg/kg/day ticarcillin in 4 doses Q6h (max 12g/day)		
TRAMADOL			
Oral/IV	1-2mg/kg (adult 50-100mg)	4-6	Maximum 400mg/24hrs
Preparations	Capsule 50mg Injection 50mg		
TAZOCIN® - Piperacillin (1g) and tazobactam (125mg)			
IV	50mg/kg piperacillin (adult dose 2-3g)	4	
Preparations:	Injection 2.25g, 4.5g		
TOBRAMYCIN			
IV	2.5mg/kg/dose (max 120mg)	8 Give as IV bolus over 3-5 minutes	Monitor levels- peak and trough at the 3rd orv4th dose
TRANEXAMIC ACID			
Oral	15-25mg/kg/dose	3	No elixir available – dissolve tablet in water and draw appropriate amount into syringe
IV	10-15mg/kg/dose	3	
Preparations:	Tablets 500mg Injection 500mg/5ml	(can use IV solution orally or topically)	

VANCOMYCIN

IV	60mg/kg/ day (max 2G)	6hourly	trough <10mg/litre
Oral	10mg/kg (adult = 125-500mg)	4	Not absorbed – no need to monitor levels

Intravenous vancomycin is not suitable for treating clostridium difficile infection. Avoid oral vancomycin for this purpose if at all possible because of risk of VRE (vancomycin resistant enterococci)

Preparations	Capsules	125mg, 500mg
	Injections	500mg – may be used orally, vials can be kept in fridge for 24 hours if for oral use.

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Rounding of Paediatric Chemotherapy Doses

Purpose/Objective

To ensure that paediatric chemotherapy doses are prepared as accurately as possible by the Pharmacy .

Intended Audience

Nursing, medical and pharmacy staff.

Associated Documents

Chemotherapy Medication Chart
Paediatric Chemotherapy Proforma/protocol
Medication Chart

Background

The pharmacy makes chemotherapy. The volume of cytotoxic agent that is able to drawn up is based on the syringe size that would normally be used for the individual drug and the graduations on that particular syringe. The chemotherapy dose should be rounded to reflect this physical restraint on measurement of drug volume.

Guideline

- Prescribers should round doses of all cytotoxic (and adjunctive) drugs as below on all paediatric chemotherapy charts or prescriptions.
- Prescribers who do **not** wish a particular dose to be rounded should indicate this clearly on the chemotherapy chart or prescription. (no guarantee is given to the required accuracy being obtained)
- Pharmacy staff will check all un-rounded doses with prescriber before rounding for production purposes.

Tablet sizes available for oral chemotherapy

Drug	Strength	Round (up or down) to nearest
Cyclophosphamide	50mg tablet	50mg
Dexamethasone	1mg, 4mg tablets, 1mg/ml soln	1mg
Etoposide	50mg, 100mg capsules	50mg
Methotrexate	2.5mg, 10mg tablets	2.5mg
6-Mercaptopurine	50mg tablet	25mg
Prednisone	1mg, 2.5mg, 5mg, 20mg tablets	1mg

Intravenous Preparations

Drug	Round (up or down) to nearest	Strength of Solution	vial/ampoule sizes
Asparaginase	200units	20000 units/ml	10000 units
Carboplatin	10mg	10mg/ml	150mg, 450mg
Cisplatin	1mg	1mg/ml	100mg
Cyclophosphamide	20mg	20mg/ml	1000mg
Cytarabine (≤ 200mg)	10mg	100mg/ml	1000mg
Cytarabine (200-1000mg)	20mg	100mg/ml	1000mg
Cytarabine (≥1000mg)	100mg	100mg/ml	1000, 2000mg
Dacarbazine	10mg	10mg/ml	100, 200mg
Dactinomycin	0.05mg	0.5mg/ml	0.5mg
Daunorubicin	5mg	5mg/ml	20mg
Doxorubicin	2mg	2mg/ml	100mg
Etoposide (Doses ≤ 200mg)	4mg	20mg/ml	100mg
Etoposide (Doses >200mg)	20mg	20mg/ml	100mg
Methotrexate Intrathecal	0.5mg	2.5mg/ml	5mg
Methotrexate	5mg	25mg/ml	100mg, 500mg
Vincristine (Doses ≤ 2mg)	0.1mg	1mg/ml	2mg

Herbal Medicines - more than harmless placebos

Adapted from an article in the New Ethicals Journal February 2001; 11-17 written by Murray Whitteker, Drug Information Service, Department of Clinical Pharmacology, Christchurch Hospital.

Introduction

Definition of a herb

In general, a 'herb' refers to a leafy plant without a woody stem that is used as a household remedy or as flavouring. We tend to consider herbal medicines as being simply any plant, plant product or mixture of plant products in any form. Indeed, plants have been utilised for their medicinal properties since the days of primitive man. It is only within the last few hundred years, with the advent of modern pharmacological sciences, that 'western' medicine has considered herbal therapy as backward or even quackery.

Patients may utilise herbal medicines for many reasons. These include: concerns about the side effects of conventional therapy, the belief that a natural product must be safe, a sense of control over their own therapy, especially where the illness is chronic or terminal, an interest in 'natural' alternatives or simply the ease of access to this type of medicine. Whatever the reason, it is safe to assume that a good proportion of patients will use herbal medicines, with or without their doctor's knowledge.

Any medicine, conventional or otherwise has the potential to display toxicity

Herbal medicines have the same propensity to cause toxicity as conventional medicines. However, herbal medicines do not undergo the extensive clinical trials or the post-marketing surveillance that helps to establish effective and safe dosage ranges and toxicity profiles.

Correctly dosed, many herbal medicines may be effective and safe, but in larger quantities they can become quite toxic. Determining the quantity of active ingredient(s) in a preparation is difficult and depends on the dosage forms (eg. dried plant, tablet, alcoholic extract or aqueous solution). In addition, factors such as the season of harvest, the geographical source of the plant, the part of the plant used and processing can all influence the quantity of active constituents.

Although many health professionals are aware of the potential hazards of herbal medicines, a public perception of safety still exists. The perception, 'that because it is natural it must be safe' is in part due to limited lay press reports describing toxicity. In turn, this may reflect the poor identification and medical reporting of herbal adverse effects and interactions. The lack of 'herbal' reporting is surprising when we consider the widespread use of herbal medicines and the range of pharmacologically active constituents they contain.

In fact many conventional medicines are plant derivatives. Consider the original source of atropine *(Atropa belladonna)*, colchicine *(Colchicum autumnale)*, codeine *(Papaver somniferum)*, cocaine *(Erythroxylon coca)*, digoxin *(Digitalis purpurea)*, quinine (*Cinchona officinalis),* senna *(Cassia acutifolia)* scopolamine *(Datura fastuosa*) and more recently, paclitaxel *(Taxus brevifolia)* and vincristine *(Catharanthus roseus*). However, as conventional medicines, the active ingredients are either isolated or synthesised, highly purified, consistently formulated and have established dosage and toxicity ranges.

Interaction with conventional medicines

Herbal medicines can interact with conventional therapy and although pharmacokinetic interactions have occurred, the vast majority of herbal-drug interactions are likely to be pharmacodynamic in nature. With a pharmacodynamic interaction, constituents of the herbal medicine will enhance or antagonise the actions of the conventional therapy (or vice versa).

By applying first principles many herbal-drug interactions should be easy to predict. For example, herbs that contain cardiac glycosides are likely to potentiate the effects of agents such as digoxin. Likewise, herbs with a diuretic action may enhance the effects of antihypertensive therapy. Unfortunately, information on the basic pharmacology, adverse effects and interactions of even common herbal medicines is quite limited.

Complicating this process further is the fact that many herbal medicines contain several active constituents, all able to individually exert actions, interact or cause adverse effects. Similarly, a number of herbal products contain multiple herbal ingredients, leading to complex pharmacology. Although undesirable, it is often necessary to base decisions on inadequate or extrapolated information.

The following represents a summary of reported adverse effects and actual or predicted interactions (1-11). It should be noted that in many instances information is limited to individual case reports and therefore causality is not always established. Caution should be exercised in the interpretation of this data.

Dong quai (Angelica sinensis)

Dong quai is used for a number of gynaecological conditions such as irregular menstruation, dysmenorrhoea, pre-menstrual tension and chronic pelvic infection.

Adverse effects

Bleeding, diarrhoea, fever, photodermatitis and phototoxicity.

Interactions

Dong quai possesses oestrogenic receptor agonist activity and may compete with receptor antagonists such as **tamoxifen,** or have additive effects with **oestrogen** replacement therapy (13).

Dong quai contains numerous coumarin and other anti-thrombotic components and may potentiate the anticoagulant effects of agents such as **warfarin** .

Dong quai contains psoralens, which may increase the risk of photosensitivity reactions. This agent may be best avoided in combination with known phototoxic agents such as **amiodarone, phenothiazines** or **tetracyclines.**

Echinacea (E. purpurea, E. angustifolia)

Echinacea is claimed to possess antiseptic and antiviral properties and it is used as a wound-healing agent and as a non-specific immunostimulant.

Adverse effects

Adverse effects appear to be rare but include somnolence, dizziness, headache, gastrointestinal disturbance, and allergic reactions such as eczema, dyspnoea and anaphylaxis.

Interactions

The immunosuppressive effects of agents such as **corticosteroids** or **ciclosporin** may be antagonised by the immunostimulating effects of echinacea.

Pyrrolizidine alkaloids, containing the 1,2 saturated necrine ring such as those contained in comfrey, have been associated with hepatotoxicity. It is suggested that echinacea, which contains similar (but unsaturated) pyrrolizidine alkaloids, should be avoided in combination with known hepatotoxic drugs. Despite widespread use, hepatotoxicity has not yet been associated with this herbal medicine .

Although echinacea contains flavonoids known to inhibit the cytochrome P-450 isoenzyme 3A4 , there are no reported interactions with this herb to date.

Ginkgo (Ginkgo biloba)

Ginkgo is claimed to improve mental alertness and overall brain function, decrease cognitive deterioration and increase blood flow. Inhalations are used in the treatment of asthma and boiled leaves are used as a treatment for chilblains.

Adverse effects

These include headache, dizziness, restlessness, seizures, nausea, vomiting, flatulence, diarrhoea and bleeding. Contact with, or ingestion of, the fruit pulp is reported to cause severe allergic reactions including erythema, oedema, blisters and itching.

Interactions

Ginkgo seeds contain the neurotoxin 4-*O*-methylpyridoxine, which may cause convulsions, loss of consciousness and death. Due to the small risk of product contamination by seeds, the use of ginkgo in patients with epilepsy is not recommended. This caution could be extended to patients receiving agents that may lower seizure threshold (eg. **bupropion, SSRI's or TCA's)**

The alkaloid ginkgolide B is a potent inhibitor of platelet activating factor-mediated thrombus formation and it may have thrombolytic activity. There are several reports of haemorrhage and/or altered bleeding times in patients receiving ginkgo . Concurrent use of ginkgo with **anticoagulants,** or in patients with known risk factors for bleeding, is not recommended.

Ginseng (Panax ginseng)

Short-term use of this herb is claimed to improve stamina, concentration, healing, stress resistance, vigilance, sexual functioning and work efficacy. Long-term use is claimed to improve well being especially in elderly patients with debilitating or degenerative conditions.

Adverse effects

These include transient nervousness, excitation, insomnia, inability to concentrate, headache, hypertension, chest pain, palpitations, epistaxis, diarrhoea, pruritus, allergy and skin eruptions. High doses or overdose is associated with headache, nervousness, insomnia, depression, palpitations, heart pain, epistaxis, diarrhoea, vomiting, rash, pruritus, skin eruptions, and amenorrhoea.

A ginseng abuse syndrome is described when large doses of ginseng are taken with other psychomotor stimulants such as coffee and tea. Associated symptoms of this include loss of appetite, euphoria and oedema.

Oestrogen-like effects such as mastalgia and vaginal bleeding have been reported in elderly, postmenopausal women taking modest oral doses or using topical applications (see case example).

Interactions

Ginseng may inhibit the uptake of various neurotransmitter substances. Headache, insomnia, tremulousness and manic-like reactions have been reported in combination with **phenelzine**. Due to the central nervous system stimulant activity of ginseng, use should be avoided in patients with conditions such as mania and psychosis.

Ginseng has been reported to decrease the INR in a patient stabilised on **warfarin**

Ginseng is reported to possess corticosteroid-like actions and the hypoglycaemic properties of this herb may complicate blood glucose control .

Ginseng may enhance the clearance of alcohol in man and there is some suggestion that ginseng may induce cytochrome P450 enzymes.

Due to its chronotropic and hypertensive actions, ginseng should be avoided in patients with cardiovascular disease. Diuretic resistance has been described in a patient taking a ginseng product containing germanium, which is present in some products .

Ginseng should not be used with **oestrogens** or **corticosteroids** due to possible additive effects .

Kava (piper methysticum)

Kava is used as a muscle relaxant, sedative, anxiolytic, calmative, anticonvulsant, antidepressant and for the promotion of wound healing.

Adverse Effects

These include sedation, oral & lingual dyskinesia, torticollis, oculogyric crisis, exacerbation of Parkinson's disease, painful twisting movement of the trunk, headache, dizziness, local numbness, gastrointestinal upset, photosensitivity, rash and eye redness. Excessive consumption may cause weight loss, altered liver function tests, photophobia and diplopia, dry, scaly skin and yellow discolouration of the skin and nails.

Although Kava produces mild euphoria, it is not thought to have any effect on thought or memory.

Interactions

The combination of Kava and other central nervous system depressants such as alcohol and the benzodiazepine alprazolam has resulted in coma.

Kava may increase the risk of extrapyramidal side effects when combined with dopamine antagonists.

Ma Huang (Ephedra sinica)

Ma huang is used as an anorexic agent, stimulant, decongestant and bronchodilator.

Adverse effects

The active pharmacological constituents of ephemera are ephedrine and its related alkaloids. The adverse effects of this herbal medicine are similar to those observed with ephedrine/pseudoephedrine. These include nervousness, insomnia, irritability, psychosis, headache, dizziness, tremor, seizures, anxiety, confusion, stroke, premature ventricular contraction, hypertension, arrhythmia, myocardial infarction, death, constipation (tannin content), exfoliative dermatitis, urine retention, kidney stones and uterine contractions.

Interactions

As expected for **ephedrine**.

Saw Palmetto (Serenoa repens)

This agent is used for its antiandrogenic and oestrogenic properties, as a mild diuretic and as a urinary antiseptic.

Adverse effects

These include headache, hypertension, nausea, abdominal pain, constipation, diarrhoea, back pain, decreased libido, impotence, dysuria and urinary retention**.**

Interactions

This agent has oestrogenic and antiandrogenic properties and may interfere with hormone replacement therapies.

This herbal medicine has been shown to inhibit dihydrotestosterone receptor binding and 5α-reductase activity. Evidence suggests that saw palmetto has efficacy comparable to finasteride in the treatment of benign prostatic hyperplasia (10). There is some suggestion however, that this agent may contribute to false-negative prostate-specific antigen (PSA) results.

Siberian ginseng (Eleutherococcus senticosus)

Siberian ginseng has been claimed to stimulate the immune and circulatory systems, regulate blood pressure, reduce inflammation, treat insomnia caused by prolonged anxiety, increase stamina and the ability to cope with stress.

Adverse effects

These include headache, insomnia, difficulty with concentrating, dizziness, euphoria, increased agitation, nervousness, hypertonia, changes in heart rhythm, pericardial pain, increased blood pressure (high doses), diarrhoea, skin eruptions, vaginal bleeding and oestrogenic effects.

Interactions

Components of this herbal medicine have been demonstrated to inhibit platelet aggregation. An increased risk of bleeding may occur when used in combination with anticoagulants such as **aspirin, warfarin** or **heparin**.

The central nervous system stimulant properties of this agent may complicate management of individuals who are highly energetic, nervous, tense, manic or schizophrenic.

Saponin constituents of Siberian ginseng may have affinity for oestrogen/progestogen and glucocorticoid receptors. There is evidence of hypoglycaemic activity that may impair glycaemic control.

The cardiovascular adverse effects of this herb suggest that it may impair the efficacy of treatments for cardiovascular disease. It has been suggested that Siberian ginseng may interfere with **digoxin** assays, producing a false elevation in concentrations.

St John's wort (Hypericum perforatum)

This is used as a herbal treatment for depression, sedation, neuralgia, fibrositis, sciatica, bronchial inflammation, burns, and as a wound-healing agent.

Adverse effects

These include neuropathy, headache, dizziness, restlessness, fatigue, sleep disturbance, confusion, mania, dry mouth, nausea, vomiting, constipation and altered liver function tests. Hypersensitivity reactions can occur including photosensitivity and pruritus.

Interactions

As an inducer of cytochrome P-450 isoenzymes, St John's wort may lower the concentrations of a number of medications. Of most concern are those agents with a narrow therapeutic index such as the immunosuppressants (eg. **ciclosporin, tacrolimus**), anticonvulsants (eg. **carbamazepine**), HIV treatments (eg. **indinavir, nelfinavir**), oral anticoagulants (eg. **warfarin**) and theophylline.

St John's wort may also decrease digoxin concentrations.

St John's wort exhibits complex neuropharmacology, but in general is considered to possess serotonin re-uptake inhibition-like activity. A risk of serotonin toxicity may occur if St John's wort is combined with drugs that increase serotonin release, inhibit serotonin re-uptake, inhibit serotonin metabolism, or stimulate post-synaptic serotonin receptors. Symptoms of excessive serotonin include changes in mental status, agitation, myoclonus, hyperreflexia, diaphoresis, incoordination, shivering, tremor, diarrhoea and fever. In some instances this may progress to cardiac arrest, coma, seizures and even death.

Additive effects may occur when St John's wort is combined with **tricyclic antidepressants**, **selective serotonin re-uptake inhibitors**, **monoamine oxidase inhibitors**, or pro-serotonergic drugs such as **carbamazepine, dextropropoxyphene, dextromethorphan, lithium, pethidine** and **tramadol.**

St John's wort may reduce the effectiveness of **coumarin anticoagulants** by enhancing their metabolism. In addition, St John's wort may also increase the risk of bleeding by depleting platelets of serotonin, resulting in reduced platelet adhesiveness.

An additive risk of photosensitivity reactions may occur when combined with agents such as **amiodarone**, **phenothiazines** or **tetracyclines**.

Documented interactions

Interacting Drug	Symptoms/effect	Suggested Mechanism
Ciclosporin	↓ concentrations	↑ metabolism
Digoxin	↓ concentrations	? effects on p-glycoprotein altering absorption and/or renal clearance
Ethinyloestradiol & desogestrel	break-through bleeding	↑ metabolism
Indinavir	↓ concentrations	↑ metabolism
Phenprocoumon, warfarin	↓ concentrations	↑ metabolism
Nefazodone, paroxetine, sertraline, trazodone	serotonin toxicity	Additive central nervous system effects
Theophylline	↓ concentrations	↑ metabolism

Valerian (Valeriana officinalis)

Valerian has been advocated for the management of restlessness and nervous disturbance of sleep. It has traditionally been used as a sedative and spasmolytic for conditions such as nervous excitability, migraine, cramp and intestinal colic.

Adverse effects

Valerian is reported to cause headache, hangover-like effects, excitability, hallucinations, increased muscle relaxation, ataxia, hypothermia, blurred vision, cardiac disturbance, gastrointestinal upset, hepatotoxicity (large doses) and hypersensitivity reactions.

Intentional overdose has resulted in rapid onset of fatigue, chest tightness, abdominal cramps, light-headedness and tremor of the hands and feet (4). A withdrawal syndrome has been reported with symptoms including cardiac abnormalities and delirium .

Interactions

Valerian has been shown to prolong **barbiturate**-induced sleep. Concomitant use should be avoided in patients taking other central nervous system depressants such as **benzodiazepines**, **opiates** and **alcohol** due to the risk of additive effects.

Miscellaneous Interactions

Chamomile (Matricaria recutita)

Chamomile contains coumarin. Despite widespread use, there are no reports however, of this translating into coagulation disorders. Caution with use of this agent is still advised in patients receiving **anticoagulant** therapy.

Feverfew (Tanacetum parthenium)

Feverfew suppresses prostaglandin production, but not via cyclooxygenase inhibition. Non-steroidal anti-inflammatories may negate the usefulness of feverfew in the treatment of migraine headache. Feverfew has been shown to inhibit platelet activity and therefore may alter bleeding time. It has an additive effect with **aspirin** and should not be used with **warfarin** or other **anticoagulants** .

Garlic (Allium sativum)

Garlic has been associated with decreased platelet aggregation and antithrombic activity. Elevations in INR and prothrombin times have occurred in patient's previously stabilised on **warfarin**. Garlic has hypoglycaemic activity and may complicate glycaemic control in some patients.

Ginger (Zingiber officinale)

As an inhibitor of thromboxane synthetase, ginger may inhibit platelet aggregation and prolong bleeding time .

Liquorice (Glycyrrhiza glabra)

When used in high doses for prolonged periods, liquorice may cause pseudoaldosteronism, which can manifest as headache, lethargy, sodium and water retention, hypokalemia, hypertension, heart failure and cardiac arrest. Liquorice should not be used in patients with liver or renal dysfunction, or cardiovascular disease.

Aldosterone-like actions of **liquorice** may offset the effects of **spironolactone** and other antihypertensive therapy. Liquorice may cause hypokalaemia, hence predisposing to **digoxin** toxicity.

Tannin

Tannin-containing herbs (eg. **feverfew, ma huang, saw palmetto, St John's wort** and **valerian**) may inhibit the absorption of **iron** .

Table of medicine – herb interactions

Herbal medicines are becoming increasingly popular and because they contain pharmacologically active constituents, it is dangerous to discount them as being harmless. Herbal medicines can cause toxicity and many have the potential to interact with conventional medicines, therefore **naturalness does not imply harmlessness.**

Herbal Medicine	Examples of Interacting Drugs	Effect
Chamomile	Anticoagulants	Increased risk of bleeding
Dong quai	Tamoxifen Oestrogens Anticoagulants Phototoxic drugs	Antagonism of effects Enhanced effects Additive risk of bleeding Increased risk of phototoxicity
Echinacea	Hepatotoxic drugs (eg. amiodarone, anabolic steroids, ketoconazole, methotrexate) Immunosuppressants	Possible additive risk of hepatotoxicity Antagonism of effects
Feverfew	Non-steroidal anti-inflammatory agents Anticoagulants	Decreased herbal effect Additive risk of bleeding
Garlic	Anticoagulants Insulin, oral hypoglycaemics	Additive risk of bleeding Additive hypoglycaemia
Ginger	Anticoagulants	Increased risk of bleeding
Ginkgo	Anticoagulants Seizure threshold lowering medications	Increased risk of bleeding Increased risk of seizures
Ginseng (Panax)	Monoamine oxidase inhibitors (phenelzine) Corticosteroids, oral hypoglycaemics, oestrogens Antihypertensives, warfarin	Headache, tremor, mania Enhanced effects Antagonism of effects
Kava	Central nervous system depressants Dopamine antagonists	Additive depressant effects Increased risk of Parkinsonism, extrapyramidal symptoms
Liquorice	Antihypertensives, spironolactone	Antagonism of effects
Ma Huang (Ephedra)	As for ephedrine	As for ephedrine
Saw palmetto	Oestrogen	Enhanced effects
Siberian ginseng	Anticoagulants Corticosteroids Digoxin Insulin, oral hypoglycaemics	Increased risk of bleeding Augmented steroid effects Assay interference Additive hypoglycaemia
St John's wort	See earlier table	
Valerian	Central nervous system depressants	Additive depressant effect