

The risk of severe salicylate poisoning following the ingestion of topical medicaments or aspirin

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Summary

Apart from isolated reports of severe salicylate poisoning after ingesting an unusually large amount of a medicinal oil, there are no published data on the threat arising from attempted suicide with topical medicaments containing methyl salicylate or wintergreen oil compared with aspirin tablets. In this retrospective study, the admission plasma salicylate concentrations and clinical presentations were compared in 80 subjects who had taken aspirin tablets ($n = 42$) or topical medicaments ($n = 38$). The proportions of subjects being symptomatic were similar in the two groups. Although the admission plasma salicylate concentrations were generally higher in subjects who had ingested aspirin tablets, the two highest readings (4.3 and 3.5 mmol/l) belonged to two of the subjects who had taken topical medicaments. Because of its liquid, concentrated form and lipid solubility, methyl salicylate poses the threat of severe, rapid-onset salicylate poisoning. The toxic potential of topical medicaments containing methyl salicylate or wintergreen oil should be fully appreciated by both physicians and the general public.

Keywords: salicylate poisoning, poisoning, topical medicament, methyl salicylate, aspirin

Salicylate poisoning remains a common problem in many Western countries with an appreciable morbidity and mortality.^{1,2} This is due largely to the ready availability of aspirin and the frequent occurrence of salicylates in unexpected sources such as cold and allergy preparations, oil of wintergreen, rubefacients for rheumatism and ointments for psoriasis.³ The more serious incidents in adults normally occur following the ingestion of large doses of aspirin in its various formulations – solid, soluble, sustained release and liquid preparations.

In Hong Kong, aspirin and other analgesics accounted for 10–18% of the adult cases of self-poisoning admitted to the Prince of Wales Hospital during 1988 to 1991.⁴ Topical medicaments containing wintergreen oil or methyl salicylate were involved in about half of the patients who were suspected to have ingested salicylates.⁵

The main objective of this retrospective study was to assess the risk of severe salicylate poisoning amongst patients who had self-poisoned themselves with topical medicaments or aspirin tablets.

Patients and methods

The Prince of Wales Hospital is the sole general teaching hospital in the New Territories East, Hong Kong, serving a population of about 1.2 million in 1994. Also situated in this region are two Vietnamese refugee camps.

From January 1991 to December 1993, all patients admitted to our general medical wards with a history of salicylate ingestion were included in the study. They were identified from our previous studies of the pattern of acute poisoning^{4,6,7} or the registry of requests for plasma salicylate measurements. Patients who had taken unknown analgesics/antipyretics but with undetectable plasma salicylate concentrations (<0.1 mmol/l) were excluded.

The hospital records of these patients were reviewed. Demographic data and information regarding agents used, clinical features, treatment given and outcome were noted. The identification of the agents responsible was based on the history from the patient/witnesses, labelling on the containers and/or the clinical features. For patients who had concomitantly taken more than one agent, only signs and symptoms that could be attributed to salicylates were considered.

Results

Eighty patients who had ingested various kinds of aspirin tablets ($n = 42$) or topical medicaments containing methyl salicylate or wintergreen oil ($n = 38$) were studied. The main reasons for self-poisoning included emotional upset, social crisis and physical illness. Psychiatric assessment indicated that three of the patients who had ingested tablet formulations were suffering from anxiety and/or depression.

As can be seen in table 1, most of the Chinese subjects included in this study had taken aspirin tablets, whereas most of the Vietnamese subjects had taken topical medicaments. Subjects who had taken aspirin tablets tended to present with mixed overdosage involving other drugs or chemicals. Six of the subjects from the topical medicament group went missing within 48 hours of admission. The two groups were

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otherwise comparable with regard to age, time lapsed between ingestion and admission to an emergency department, the use of gastric lavage or ipecac, the proportion having symptoms of salicylate poisoning and duration of hospital stay. The alleged amounts of aspirin or salicylates ingested by the two groups of subjects are summarised in table 2.

Table 1 Clinical details of 80 subjects who self-poisoned themselves with two different formulations of salicylates

	Tablets (n = 42)	Topical medicament (n = 38)
Men: women ratio	8:34	7:31
Chinese subjects	39 (93%)	4 (10%)
Vietnamese subjects	2 (5%)	34 (90%)
Age (years)	22 (15–80)*	22 (15–86)*
Ingestion–admission intervals (h)	3 (0.5–48)*	3 (0.5–16)*
Mixed overdosage	27 (64%)**	10 (26%)†
Gastric lavage/ipecac	32 (76%)	29 (76%)
Plasma salicylate levels (mmol/l)		
not requested	1 (2%)	0
< 0.1	4 (10%)	13 (34%)
0.1–1.0	13 (31%)	18 (48%)
1.1–2.1	16 (38%)	5 (13%)
≥ 2.2	8 (19%)	2 (5%)
Severity of salicylate poisoning††		
no symptoms	17 (40%)	13 (34%)
mild	24 (58%)	24 (64%)
moderate to severe	1 (2%)	1 (2%)
Duration of stay (days)	2 (1–4)*	2 (1–5)*
Outcome (%)		
found missing	0	6 (16%)
discharge against medical advice	3 (7%)	1 (3%)
transferred to other units	2 (5%)	1 (3%)
home	37 (88%)	30 (79%)

*Medians and ranges. **Other agents included paracetamol or paracetamol-containing drugs (n = 13), hypnotics (n = 7), alcohol (n = 7), Chinese proprietary medicines (n = 4), tricyclic antidepressants (n = 2), antacids (n = 2), and household products (n = 2). †Other agents included alcohol (n = 4), antibiotics (n = 3), paracetamol (n = 2), and household products (n = 2). ††Symptoms including nausea, vomiting, tinnitus, deafness, sweating, hyperventilation and respiratory alkalosis/metabolic acidosis.

The plasma salicylate concentration in relation to the time of ingestion is shown in the figure. Twenty-four subjects were excluded because the test was not requested (n = 1), the time of ingestion was not known (n = 6) or plasma salicylate concentrations were below 0.1 mmol/l (n = 17). In the 11 patients who had two or more measurements (six had taken aspirin tablets), the highest plasma level was used for analysis. Subjects who had taken aspirin tablets tended to have higher plasma salicylate concentrations than subjects who had taken topical medicaments, although the two subjects with the highest levels belonged to the latter group.

Urinary alkalisation⁸ was considered necessary in the two patients with moderate to severe symptoms of salicylate poisoning after ingesting 30 'Anacin' tablets (plasma salicylate con-

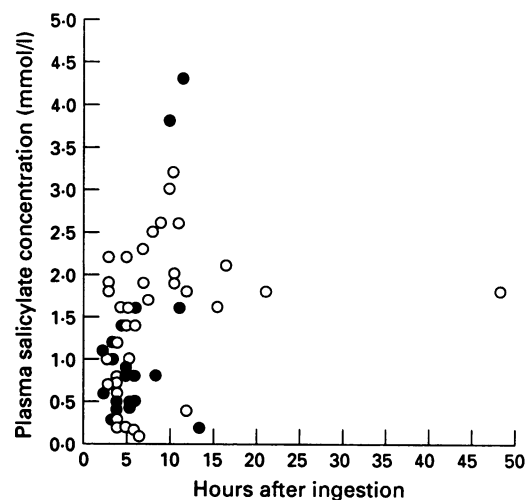


Figure Plasma salicylate concentration in relation to the time of ingestion in 56 subjects who had taken aspirin tablets (O, n = 36) or topical medicaments (●, n = 20).

Table 2 The alleged amounts of aspirin tablets or topical medicaments ingested by 80 subjects

Dosage form	Quantity
<i>Tablet formulations (n = 42)</i>	
Cortal (n = 21)	≤ 10 tab = 8; 11–20 = 11; ≥ 21 = 1; NK = 1
Anacin (n = 8)	≤ 10 tab = 3*; 11–20 = 2; ≥ 21 = 2; NK = 1
Aspirin** (n = 4)	≤ 10 tab = 1; ≥ 21 = 1; NK = 2
Coricidin (n = 1)	11–20 tab = 1
Excedrin (n = 1)	11–20 tab = 1
Unspecified (n = 7)	11–20 tab = 1; ≥ 21 = 2; NK = 4
<i>Topical medicaments (n = 38)</i>	
White Flower Medicine Oil (n = 22)†	≤ 10 ml = 5; 11–20 = 2; ≥ 21 = 2; NK = 13
Red Flower Oil (n = 5)	11–20 ml = 1; NK = 4
Axe Brand Universal Oil (n = 1)	11–20 ml = 1
Black Man Oil (n = 1)	NK = 1
Unspecified medicated oils (n = 9)	≤ 10 ml = 1; 11–20 = 2; ≥ 21 = 2; NK = 4

NK = not known. *One subject also took two aspirin tablets. **The strength of the tablet was not specified. †One subject also took an unknown amount of an unspecified medicated oil.

Cortal (acetylsalicylic acid 500 mg, caffeine 30 mg), Anacin (aspirin 400 mg, caffeine 32 mg), Coricidin (chlorpheniramine 2 mg, acetylsalicylic acid 388.8 mg, caffeine 32.4 mg), Excedrin (acetaminophen 250 mg, aspirin 250 mg, caffeine 65 mg). White Flower Medicine Oil (wintergreen oil 40%, menthol crystal 30%, eucalyptus oil 18%, camphor 6%, lavender oil 6%), Red Flower Oil (wintergreen oil 67%, turpentine oil 22%, cinnamic aldehyde 5%, cinnamon leaf oil 4%, citronella oil 2%), Axe Brand Universal Oil (methyl salicylate 15%, menthol crystals 20%, eucalyptus oil 15%, essential oil 12%, camphor 5%), Black Man Oil (wintergreen oil 28%, turpentine oil 70%, thymol crystal 1%, citronella oil 1%).

centration 1.9 mmol/l seven hours post-ingestion) or an unknown amount of 'Red Flower Oil' (4.3 mmol/l at 11.5 hours). One patient who had taken a tricyclic antidepressant and 'Cortal' was initially managed in the intensive care unit because of respiratory depression and aspiration pneumonia. One patient who had taken aspirin with an opioid antitussive also required admission to the intensive care unit. One patient who had taken paracetamol and 'Cortal' was given a full course of intravenous *N*-acetylcysteine because of a toxic plasma paracetamol concentration.

Ten patients discharged themselves prematurely or disappeared from wards before their symptoms had completely subsided. The remaining 70 patients made a complete recovery.

Discussion

Methyl salicylate or wintergreen oil is an important cause of acute salicylate poisoning in Hong Kong.^{5,7} This is due largely to the ready availability of a wide range of topical medicaments used in the self-treatment of conditions such as musculoskeletal pains and the common cold. The lack of a warning in the package inserts may also have contributed to their popularity in deliberate self-poisoning.⁹

In salicylate poisoning, the dose ingested and the age of the patient are the most important factors which determine severity.³ Classification of toxicity (asymptomatic, mild, moderate, severe) may be made on clinical observation of the patient and plasma salicylate concentrations. Neurologic disturbances such as confusion, delirium and coma are the best clinical indicators of severe poisoning.¹⁰ They usually occur when metabolic acidosis is the dominant acid-base abnormality and are due to reduced ionisation of salicylic acid and a shift of salicylate from plasma into the brain.¹⁰ Dominant metabolic acidosis is most common in young children, who are, therefore, more likely to experience serious intoxication at relatively low plasma salicylate concentrations.

Methyl salicylate poses the threat of severe, rapid-onset salicylate toxicity because of its liquid, concentrated form.¹¹ To put into perspective the danger of this compound, one teaspoon of wintergreen oil (98% methyl salicylate) is equivalent to approximately 7000 mg of salicylate or 21.7 adult aspirin (325 mg) tablets.¹² However, in view of its lipid solubility, methyl salicylate is expected to be more toxic than aspirin.¹³ Ingestion of as little as 4 ml in a child and 6 ml in an adult have been

fatal,¹⁴ although the lethal dose in adults is estimated at 30 ml.^{14,15} Ingestion of 100 ml of one brand of 'Red Flower Oil' (methyl salicylate content not known) has been reported to cause severe salicylate poisoning (initial plasma salicylate level 9.6 mmol/l).¹⁶ The toxic potential of topical medicaments may also be due to other ingredients such as camphor and turpentine oil.

Apart from the isolated report mentioned above,¹⁶ there are no published data on the threat to the average parasuicide patient who had ingested topical medicaments compared with aspirin tablets. To quantify this relative risk, the dose of salicylates ingested must be known. However, such information was not available in many of our patients who had ingested topical medicaments. There might be several different manufacturers of products of the same or similar brand name. Some products are available in several different size packs, eg, 2.5 to 60 ml in the case of 'White Flower Medicine Oil', but the size of the bottle involved was seldom specified.

In this study, the proportions of subjects having symptoms were similar in the two groups (table 1) although the plasma salicylate concentrations (figure) were generally lower in subjects who had ingested topical medicaments. However, as two of these patients also had the highest plasma salicylate concentrations, the potential dangers from these products, particularly those with a high methyl salicylate content, should not be underestimated.

Two factors may possibly explain why severe poisoning was not seen more frequently amongst subjects who had taken topical medicaments. Many of the subjects in the

Features of salicylate poisoning¹⁰

- common: nausea, vomiting, tinnitus, deafness, sweating, hyperventilation, respiratory alkalosis/metabolic acidosis
- uncommon: coma, fever, hypoglycaemia, hypokalaemia, gastrointestinal haemorrhage, fluid retention, pulmonary oedema, respiratory distress syndrome, cerebral oedema, renal failure

Management of salicylate poisoning¹⁸

- gastric emptying if > 4.5 g taken by an adult or > 2 g by a child within 4 h
- activated charcoal
- measurement of plasma salicylate concentration in those with symptoms
- arterial blood gas analysis in those with severe poisoning or high plasma salicylate concentrations
- supportive measures
- enhanced elimination of absorbed salicylate

Minor toxicity (plasma salicylate concentrations < 350 mg/l (2.5 mmol/l) in children and < 450 mg/l (3.3 mmol/l) in adults): increase oral fluid intake

Moderate toxicity (plasma salicylate concentrations 350–700 mg/l (2.5–5.1 mmol/l) in children and 450–700 mg/l (3.3–5.1 mmol/l) in adults): repeated doses of activated charcoal plus urinary alkalisation

Severe poisoning (the presence of CNS features including delirium, extreme agitation, confusion, coma and convulsions, the presence of acidaemia or plasma salicylate concentrations > 700 mg/l (5.1 mmol/l): correct acidaemia, repeated doses of activated charcoal, consider haemodialysis

topical medicament group (predominantly refugees) disappeared from wards shortly after admission. These subjects might have swallowed only a small amount in order to come to hospital, from where they could escape. The amount ingested obviously depended on the size of the bottle available to the subject at the time of self-harm. 'Red Flower Oil' poses a greater threat than 'White Flower Medicine Oil' as it has a higher methyl salicylate content ($\geq 60\%$ vs $\leq 40\%$)^{9,16,17} and is available only in bottles of > 60 ml.

The toxic potential of topical medicaments containing methyl salicylate or wintergreen oil should be fully appreciated by both physicians and the general public. Including an adequate warning in the package insert and restricting the sizes of the bottle available (eg, to under

Summary/learning points

- because of its liquid, concentrated form and lipid solubility, methyl salicylate poses a threat of severe, rapid-onset salicylate poisoning
- the toxic potential of topical medicaments containing methyl salicylate should be fully appreciated

Box 3

10 ml) may help to reduce the threat of serious salicylate poisoning.

I wish to thank my colleagues at the Prince of Wales Hospital for allowing me to study their patients.

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