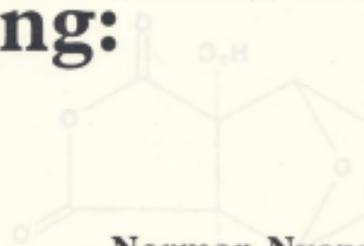


Cantharidin Poisoning: A Review



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Curriculum vitae

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In almost all parts of the world where the blister beetles are found, they are or have been employed for medicinal purposes because of the effects of the active principle, cantharidin (Fig 1). There are several species of the blister beetle found in southern Africa that contain a significant amount of cantharidin. There are about forty species of the beetle which belong to the three genera, *Decapoloma*, *Mylabris* and *Cynollyta*¹. The most widely distributed genus is *Mylabris* and the most commonly used species in this genus is *Mylabris alternata* (Fig 2). The

Summary

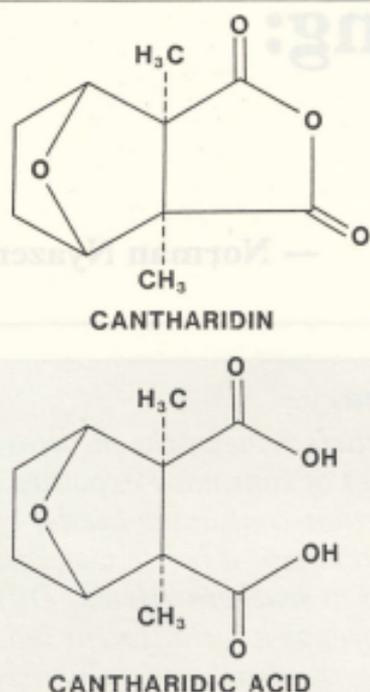
This article reviews the medical consequences of continued exposure to cantharidin-containing beetles of the *Mylabris* spp, a beetle widely distributed in southern Africa. Different ethnic groups have different indications for the dried and pulverised beetle. Among most of them it is used commonly for all types of abdominal pains, with toxic effects on the liver, the gastro-intestinal and urinogenital tracts, the cardiovascular, reproductive and nervous systems. Presenting symptoms and recommended treatment is given.

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medicinal uses of cantharides as the powdered beetle have been well documented in medical literature^{1,2,3,4,5}. Universally, cantharides were used for their aphrodisiac properties or as a cure for impotence. In southern Africa, the insect is used by traditional medical practitioners for constipation and unspecified abdominal pains (this is the major use in view of the importance attached to bowel function), as an abortifacient and to treat sexually transmitted diseases such as gonorrhoea^{1,5}. These and other therapeutic uses of the blister beetles have been overshadowed by the reported cases of acute toxicity due to ingestion of the powdered insect^{6,7,8}. Patients often present with vomiting, epigastric pain, bloody diarrhoea and frank haematuria.

Fig. 1



These reported cases of poisoning by cantharides have stimulated interest in the field of pharmacology. Research in the field has been focused on the quantification and qualification of the toxic principle in the beetle^{9,10,11,12}. All studies agree that the toxicity of the beetle is due to cantharidin, an acid anhydride of cantharidic acid. Various methods of extraction employed have shown that different species of the beetle contain different amounts of cantharidin. *Mylabris pustulata* contain 2% of dried cantharidin¹³; *Cynollyta sapphirina* yielded 1,0%¹⁰ and *Cantharis vesicatoria* gave 0,6%¹³. The lowest yield was obtained from *Epicauta pestifera* 0,3%¹². The Zimbabwean strain of *Mylabris alternata* studied showed a 0,55% content of cantharidin in the dried cantharides⁹.

Recommended Treatment

The recommended treatment for these poisonings is emptying of the stomach by inducing emesis or by aspiration and lavage and the use of activated charcoal and sodium sulphate. The patient must also be given demulcent drinks freely (but not oils or fats) analgesics, and anti-inflammatory agent such as hydrocortisone.

Uses

Before the toxic effects of cantharidin had been brought to light, the compound was once legally formulated and marketed in various pharmaceutical dosage forms for a variety of purposes. A once common product was cantharone, a 0,7% colloid of cantharidin which was used for the

treatment of warts. The anti-cancer action of cantharidin that has been demonstrated in mice, seems to support its use as a wart remover². Other pharmaceutical products of cantharidin, which have since been phased out because of toxicity, are:-

- i) Pulvis cantharides — the powdered blister beetle.
- ii) Cestan cantharidis — cerate of blister beetle which was used externally in the form of wax or ointment.
- iii) Tincture of cantharides, a 10% mixture of cantharides in alcohol and castor oil.
- iv) Collodion picis cantharidum — used externally as cantharidin pitch plates.
- v) Cantharidin ointment in benzoated lard — once used as a dressing to produce vesication.

Blister beetles are still used worldwide for medicinal purposes

The main actions for which cantharidin was used besides as an aphrodisiac, were its vesicant, counter-irritant and rubefacient actions^{3,12,14}. With respect to its counter-irritant action, the compound was used long ago for treatment of pleurisy, pneumonia, arthritis and various dermatological conditions¹⁵. It has been used as the active ingredient in hair tonics for its rubefacient effect.

Toxicity

Experience around the world has shown that the toxic effects of the blister beetle are clinically more important than the supposed therapeutic effects. Many of the reported cases were of ingested cantharidin or cantharides. Percutaneous absorp-



Fig. 2: *Mylabris alternata*.

tion of cantharidin leading to systemic toxicity must not be under-rated since its high lipoid/water partition coefficient permits rapid diffusion across the stratum corneum. A case of systemic poisoning after contamination of the skin has been reported in a 22 month old child⁷.

Gastrointestinal tract

Cantharidin has a blistering effect on the mucous membranes. After oral administration, a severe burning pain is felt involving the lips and throat. Cantharidin 175 mg, when swallowed, corrodes the oesophageal lining, making swallowing very painful. Crampy abdominal pains caused by the excoriating, blistering and ulcerating effects of cantharidin on the gut mucosa have been reported. It is the direct effect of cantharidin on the gut mucosa that stimulates gastric motility leading to increased influx of water into the gut lumen which causes the diarrhoea.

● *Patient*

A 25 year old man admitted to Parirenyatwa Hospital, slowly recovered after ingesting half a teaspoon of cantharides powder to treat urethral discharge. One hour after swallowing, the man started vomiting, followed by bloody diarrhoea. He responded to treatment including IV fluid plus tetracycline, stomach wash and pethidine.

Urinogenital tract effects

The most common systemic toxic effect of cantharidin is renal damage^{6,8}. Post-mortem examination of the kidneys of one victim of cantharidin poisoning revealed gross haemorrhage into the tubules with damage to the tubular epithelium⁶. Severe inflammation and vascularisation of the genito-urinary tract of rats were

Before the toxic effect was discovered it was very widely used for a variety of purposes

observed following chronic exposure to cantharidin. The damage to the nephron leads to glomerulonephritis and glomerular necrosis which is manifested as haematuria and proteinuria^{7,8}. Cantharidin also irritates the urinary bladder leading to increased contractile frequency of the detrusor muscle. In men, the compound irritates the urethra and together with its rubefacient action causes increased blood flow to the penis leading to severe priapism. Prolonged severe

priapism can lead to impotence due to the permanent penile damage that results¹⁶. In females, peri-pelvic and periuterine haemorrhage has also been reported.

● *Patient*

A 36 year old man went to a nganga for treatment of dysuria and umbilical abdominal pain. He was given an unknown amount of cantharides powder to drink and developed haematuria shortly after. When he was brought to Parirenyatwa Hospital, he had developed a severe headache. He responded to treatment with IV fluid, magnesium trisilicate and paracetamol.

Today the toxic effects are regarded as more important than the therapeutic effects

Cardiovascular effects

Cantharidin has been reported to have arrhythmogenic and cardiotoxic effects after systemic absorption. The arrhythmias associated with high doses of the compound were frequent ventricular ectopics, tachycardia, fibrillation or asystole. The tachycardia was thought to be a compensatory mechanism of the body to the cantharidin induced hypotension^{6,7}. On the ECG, cantharidin cardiotoxicity showed as deformed P waves, elevations of the ST segment, waxing and waning of T waves and transient T inversion. Cantharidin-induced toxic atrial fibrillation was responsible for P wave deformation while the other ECG changes were due to toxic myocarditis. Fatal arrhythmias in cantharidin poisoning could not be explained by any electrolyte change in the blood and are suggested to be due to the direct cardio-toxic action of the drug. Sudden death was attributed to ventricular dysrhythmias⁷.

● *Patient*

An 18 year old woman, who swallowed about 2 ml of a preparation containing cantharidin, developed electrocardiographic changes indicative of myocardial damage, in addition to local effects in the mouth, throat and pharynx, which responded to treatment with hydrocortisone, sodium succinate and with ampicillin¹³.

Reproductive system

Toxicity of cantharides on the rat foetus has been demonstrated⁹. Cantharidin has been shown to

cause contraction of the isolated uterine muscle. However, this does not mean that this is what happens in an intact animal. This has been confirmed by results from pregnant mice which were given oral doses of cantharidin. Cantharidin did not induce abortion in these animals but *in utero* death of the foetus. In this respect, the employment of cantharidin by traditional healers in Zimbabwe as an abortifacient, is questionable. However, the cantharides powder is very popular among males who use it as an aphrodisiac with dire consequences.

● Patient

A 31 year old man presented at Parirenyatwa Hospital, with a persistent erection, haematuria, diffuse pain in the abdomen and headache. The priapism responded to aspiration and diazepam. The patient was also put on high fluid intake.

Hepatotoxicity

The hepatotoxicity of cantharidin has been reported. Varying degrees of hepatic parenchymatous degeneration and loss of cell individuality because of distortion of cytoplasmic borders, has been shown⁸. Scattering of bile pigment containing hepatocytes and also an interstitial oedema with slight fatty changes in the liver have been observed⁶.

Nervous system

Rare cases of fatal clonic convulsions and loss of consciousness due to the drugs have been reported^{6,7}. Two patients who developed a Guillain-Barre type of flaccid paralysis two weeks after acute toxic effects of cantharidin and subsided, were reported in Johannesburg¹⁷.

Cantharide-powder is very popular among black males as an aphrodisiac — with dire consequences

Comment

Physicians practising medicine among Blacks in southern Africa should continue to be aware that many of their patients use traditional remedies. This usually happens well before the patient comes to consult the western type of health system. Poisoning may occur during this time as an untoward effect in the normal use of the traditional remedy or of incorrect use. Unfortunately, patients come to hospital when it is too late to do anything when much damage has already been done.

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Several species of the blister beetle found in southern Africa contain large amounts of cantharidin

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