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A Review of the Use of Lead Compounds in Medicines, Cosmetics and Food Additives

A. D. Hardy[1] and R. Vaishnav[2]

[1]College of Science, Sultan Qaboos University, P.O.Box 36, Al-Khod 123, Muscat, Sultanate of Oman. [2]College of Medicine, Sultan Qaboos University, P.O.Box 35, Al-Khod 123, Muscat, Sultanate of Oman.

استعراض لاستخدام مركبات الرصاص الموجودة بالأدوية ومستحضرات التجميل والمواد المضافة للأطعمة

راجيني فيشناف وأندرو هاردي

خلاصة : هذه الدراسة هي مراجعة شاملة لاستعمالات مركبات الرصاص في الأدوية وأدوات التجميل والمواد المضافة للأطعمة والأشربة . وتغطي الأمثلة التي هي من مختلف مناطق العالم حقبة طويلة من الزمن ، كما تغطي الاستعمالات الحالية لهذه المركبات ، مركبات الطب الشعبي ومستحضرات التجميل في دول الشرق الأوسط .

ABSTRACT: A review on the usage of lead compounds in medicines, cosmetics and food/drink additives is presented. Examples cover a large time-scale (from antiquity to the present day) and come from many parts of the world. Only examples where lead compounds have been *deliberately* added are covered in this review. Lead's toxicology is briefly mentioned, as is the *current* usage of lead compounds in *traditional* remedies/cosmetics in the Middle Eastern countries.

The fall of the Roman Empire, the change in the painting style of Francisco de Goya and the increase in use of wigs by Elizabethan ladies - all of these are thought to be caused, at least partially in the first two examples, by lead poisoning. As regards the Roman Empire; the story of the 'sapa', a ubiquitous lead-containing Roman sweet sauce, is told by Emsley (1994). The change in the painting style of Goya, and its possible lead-related reason, is mentioned in "Lead is a Silent Hazard" (Stapleton, 1994); and the details of the use of Venetian ceruse a (mixture of white lead and vinegar) as a face cosmetic in the sixteenth century - and its effects on hair - are told by Nriagu (1983). Also, very recently, a popular American magazine (Lemonick, 1996) has suggested that Ludwig Van Beethoven's deafness may have been caused by his consumption of mercury or lead compounds as a 'cure' for one of several real/perceived illnesses (he did suffer from terrible diarrhoea). An ongoing analysis of some of his death-bed hair should be able to provide an answer to this suggestion.

More mundanely, and more recently, there are occupational and non-occupational sources of lead poisoning. Occupationally there are the workers, and sometimes their families, in: lead-acid battery plants, lead smelters, lead mines, the manufacture of lead-based pigments/paints/glazes, the manufacture/use of 'printers' type metal (85% lead, 11% antimony and 4% tin) and the hazards associated with often home-based arts and crafts/hobbies (e.g. making and working with lead glass, and in rubber-mould making - the curing agent being used was lead peroxide). Also, painters still using lead-based pigments and potters still using lead-based ceramic glazes, can be exposed to significant levels of lead in their work.

Non-occupationally there are many possible sources of lead poisoning; ranging from contamination of illicit drugs/liquor (usually from the lead solder in the containers used in their 'manufacture') to sniffing of leaded gasoline by adolescents to drinking water that has been carried or stored in leaded pipes/containers (especially if the water is soft and slightly acidic). Also, documented lead poisoning cases have arisen from: drinking from earthenware containers which had a lead-based ceramic glaze (e.g. Bird et al., 1982); lead bullets in inoperable places in the human body (e.g. DiMalo and Garriot, 1980); and from the use of the many traditional remedies/medicines/cosmetics still available in many parts of the world (for summaries see: Stapleton, 1994;World Health Organization; WHO, 1995).

Review

The deliberate use of lead-based compounds as medicines (traditional or otherwise), cosmetics and food

additives has a long and lethal history. Some examples are:

To ward off evil, in an ancient culture, sometimes involved writing a spell on "paper" with red ink. The red ink symbolised blood. If the "paper" was then burnt and the ashes swallowed it was believed that the evil would be removed. Unfortunately the red ink was usually made from red lead (Pb_3O_4), so the most probable 'answer' to the spell would be for the swallower to come down with lead-induced colic (Nriagu, 1983).

As early as 400 BC, Hippocrates, in a text on the treatment of ulcers (Angelotti and Martini, 1997) mentions the use of lead several times- as an ingredient for powder or liquid medicines.

Lead compounds have long been used for the artificial darkening of hair (the lead reacts with the -SH functional groups in the hair to form black lead sulphide in the hair shaft). Such hair dyes were probably popular with the women of ancient Italy and the Middle East; and certainly by: the men of ancient Germany using a soap, "litharge of silver" for reddening the hair, by various peoples in the Middle Ages (using a thick paste of litharge, burnt lime and chalk), by the Victorians in England (using lead acetate) and as recently as the 1970's several brands of shampoo contained lead sulphide (Nriagu, 1983).

Several lead compounds were used as beauty aids in China, both in antiquity and during the Middle Ages. Tradition generally attributes the invention of the white lead (basic lead carbonate; $2\,PbCO_3.\,Pb(OH)_2$) cosmetic to the High King Chou - last ruler of the Shang dynasty (1520 - 1030 B.C). A mixture of three parts fine rice powder and one part white lead was used to whiten not only the faces of Chinese ladies, but also their backs, shoulders and breasts. Also, a cosmetic based on red lead was used to give rosy cheeks; and later, when yellow became a fashionable colour for the forehead, the yellow cosmetic used was often made from yellow lead oxide (PbO) (Nriagu, 1983). Currently, Chinese herbal medicines can often contain lead compounds and so give rise to poisonings; several case studies are listed by De Smet et al. (1992).

White lead was used to give a 'pale allure' to the skin for centuries. In the 17th century it was mixed with chalk and the resulting mixture used to saturate wool, which was then used to apply the powder to the face. This preparation was called "Spanish wool". A later variation was "Spanish papers", where a small note pad contained leaves made from wool, which had been saturated with white or red paint. Both such paints, in that time period, were usually based on lead compounds. "Spanish Papers" were readily portable and so were one of the earliest versions of today's powder compact (Scott, 1997). Also, even though the hazards were known white lead was being used by society ladies in England in the 1700's. In 1766 author Horace Walpole wrote "that pretty you woman, Lady Fortrose, Lady Harrington's eld daughter, is at the point of death, killed, like L Coventry and others, by white lead, of which noth could break her" (Johnson, 1993).

In 1767 in England, "Devonshire colic", which been killing workers in Devon, was identified as poisoning caused by a strong local drink (Johnson, 19 Initially the lead poisoning arose from the lead linin presses and vats being used. Unfortunately a later h developed where lead acetate (also called sugar of l was deliberately added to the drink in order to sweet The related practice of sweetening cheap wine with acetate was one of the reasons for the introduction i UK, in the 1860's, of the world's first food legisl (Taylor and Williams, 1995).

At the turn of the century, large numbers of peo Philadelphia, U.S.A, were poisoned by bakers a lead chromate as a food colouring agent in their b goods (Stapleton, 1994). Also, at the start o industrial revolution in the U.K., lead chromate popular yellow colourant for sweets, custards and (Mann, 1992).

A criminal case of lead poisoning occurr Hungary recently when red lead had been delibe added, as a colourant, to some old paprika spice in to make it look fresh. Several dozen people hospitalised with lead poisoning, and the Hun government was forced to temporarily ban the spice and order a recall of all stocks in shops so they co analysed for lead content ("The Independent", 19

The use of lead-based traditional remedies ha an ancient practice both in India and Pakistan; 'K are traditional remedies (often of ancient origin currently used in the Indo-Pakistan sub-contine variety of diseases. Unfortunately, a number contain 'heavy' metals (that is metals with a densi g/c.c.), including lead (e.g. Aslam et al., 1979; I Asghar, 1989).

Various lead compounds are currently use Mexican folk remedies 'azarcon' (Pb_3O Lead/Minium/Lead peroxide/Lead tetroxide), ($PbCO_3$; lead carbonate). All are used to treat 'e (whose symptoms are often diagnosed by phys gastroenteritis) (Baer and Ackerman, 1988) poisoning can result from the use of these tr remedies (e.g. Cueto et al., 1989).

The current use of traditional remedies by in groups in developed countries, has also been re addition to some cases from the previous two traditional medicines). A lead-containing prescribed for diabetes and haemorrhoids, ca poisoning in two adult Asian Indian immi Canada (Pontifex and Garg, 1985). Also,

herbal medicine, prescribed for haemorrhoids to a Korean woman living in the UK, resulted in chronic lead and arsenic poisoning (Mitchell-Heggs et al., 1990). Very recently, in the U.K., five case studies have been presented of lead poisoning from traditional Asian remedies. In three of the five cases the remedies had been prescribed for impotence or infertility (Bayly et al., 1995).

In the GCC countries the traditional remedies Bint Al Dhahab (a mixture of lead oxides, polymorphs of PbO (Worthing, Sutherland and Al-Riyami, 1995) given to new-born babies and small children for clearing the meconium and for stomach ailments), Saoodt and Cebagin (lead-containing teething powders) have all been *currently* implicated in cases of lead poisoning (e.g. in Oman, for Bint Al Dhahab; Sharma et al., 1990 Wolf, 1990). Also, the practice of "Bokhoor" should be mentioned; this is where 'a substance' is burnt in a fire and the resulting fumes inhaled in the mistaken belief that it will calm/cure/ward off the evil-eye in irritable infants and children. The use of lead, or a lead compound, in this ritual has resulted in deaths (e.g. in Kuwait, Shaltout et al., 1981).

Also, kohls are a type of traditional remedy long-used in the GCC countries; they are primarily used as eye cosmetics but have other uses. For example, kohl is sometimes applied to the stump of the umbilical cord of a new-born infant in order to 'protect' the child from future harm (i.e. to ward off the evil eye and for its supposedly astringent action). Kohls are often in the form of a fine black powder, although other colours and forms do exist. They *can* contain lead (often lead sulphide, the ore galena, see Parry and Eaton, 1991; Al-Hazzaa and Krahn, 1995). The authors of this review have published a detailed report on the usage of kohls in general, and on the composition of kohls available in Oman in particular (Hardy et al., 1998).

Eye cosmetics are as old as vanity, and when kohls are used as such in Oman they are applied to give beautification, to ward off the evil eye and in the belief that they are beneficial for the eyes (i.e. to relieve eyestrain, pain or soreness). They are often deliberately placed *inside* the eye. They are primarily used on infants, and by persons of both genders in the rural areas of Oman; around Muscat it is rare for them to be used by men. In the Arab world eye make-up is called kohl, in India it is called surma or kajal and in Nigeria the word used is tiro.

Exposure to inorganic lead produces a variety of pathological changes in different organ systems and these differ in presentation in adults and in children. Adults absorb 5 to 15% of ingested lead and retain < 5% of what is absorbed. Children have a greater absorption capacity than adults. They absorb 41% of ingested lead. Once lead is absorbed, about 99% of it is bound to haemoglobin. From the blood inorganic lead is initially distributed in the soft tissue of the body, particularly in the kidney and liver. Eventually most of the lead is redistributed to the bone and the half-life of this pool of lead is more than 20 years (Klaasen, 1996).

Inorganic lead also accumulates in the brain; specifically in the grey matter and in the basal ganglia (Hardman and Limbird, 1996). The most serious manifestation of lead poisoning is lead encephalopathy, often seen in children. The younger the child the more severe are the clinical signs and the prognosis is poorer. Chronic exposure to low levels of lead produces mental deterioration and such sub-clinical toxicity in children is currently a cause for concern. Lowered intelligence quotients, learning disabilities and behavioural abnormalities in children are now being attributed to chronic lead poisoning (Needleman et al., 1990). Blood lead levels of ≥ 10 μg/dl in children are the currently acceptable figures indicative of excessive lead absorption (Hardman and Limbird, 1996).

Another target for the toxic effects of lead is the haematological system. Hypochromic microcytic anaemia is a common observation in children with chronic lead poisoning. This is due to a decrease in the life span of erythrocytes and an inhibition of haem synthesis. The enzymes involved in the biosynthesis of haemoglobin that are inhibited by lead are δ-aminolaevulinic acid dehydratase and ferrochelatase. Higher blood lead concentrations are known to result in basophilic stippling of the erythrocytes.

Lead also effects the smooth muscle of the gut and produces vague abdominal symptoms that are early signs of lead toxicity. Severe lead colic is a feature of advanced poisoning.

The widespread use of lead containing kohls in the Middle East should be considered as a definite source of potential lead poisoning. New born children and infants are a particularly high risk group. Infants receiving breast milk can be exposed to toxic concentrations of lead, as lead is secreted into the milk of lactating mothers who apply lead-based kohls on a regular basis (Al-Khawajah, 1992).

The nasolacrimal duct is probably the main route of entry of lead following kohl application in the conjunctiva of the eye. The oral route, consequent to contaminated finger licking, cannot be excluded as a possible port of entry for lead. This route could hence be an important one, and may cause lead intoxication irrespective of whether kohl is applied in or around the eye, on other parts of the face, on the umbilicus or elsewhere.

Current opinion on "safe" exposure levels of lead in children is somewhat uncertain, and varies from country to country (Klaasen, 1996). Recent evidence suggests that children with a body burden below that giving rise to overt toxicity have lowered intelligence quotients and behavioural abnormalities (Needleman et al., 1990).

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Hence children in the Middle East exposed to continuous small doses of lead from traditional remedies may not only have intelligence deficits but may later develop serious central nervous system toxicities.

Conclusions

Lead serves no known useful purpose in the body. This review has shown that lead compounds have been extensively used in the past as medicines, cosmetics and food/drink additives. Even in the *present day* some usage does occur, mainly in developing countries and in ethnic minorities in developed countries. Further education is needed to prevent these toxic substances from being used in the future; with special concern being given to the elimination of their use in children.

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