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Presence of drugs in different tissues of an Egyptian mummy

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Abstract. Data are presented on the biochemical findings in several internal organs from an Egyptian mummy with a ^{14}C-dating of approximately 950 B.C. By use of radio immunoassay systems and gas chromatography/mass spectrometry, significant amounts of various drugs were detected in internal organs (lung, liver, stomach, intestines) as well as in hair, bone, skin/muscle and tendon. These analyses revealed a significant deposition of tetrahydrocannabinol (THC), nicotine (and its metabolite cotinine) and cocaine in the tissue from the mummy. The concentration profiles additionally provide evidence for the preferential ways of consumption: Thus, the highest levels of THC in lung specimens point to an inhalation of this drug – as it has been assumed from known ritual smoking ceremonies –, while nicotine and cocaine containing drugs showed their highest concentrations in the intestines and liver, so that they seem to have been consumed perorally. Furthermore, a histopathological examination of the internal organ tissues revealed some evidence for the underlying disease and the probable cause of death. Thus, a severe and presumably recurrent intravital pulmonary bleeding, most obviously due to a parasitosis affecting the lung, was observed.

Introduction

At present, the consumption of significant amounts of drugs can be monitored by specific drug measurements or by analysis of their metabolites in various body fluids [1]. This procedure is usually applied to present drug addicts. For monitoring of patients, these techniques have been adapted to tissue specimens [2] and hair [3, 4]. In our previous studies we have used this methodology to analyse historic tissue samples [5–8]. Hence, we have provided circumstantial evidence that some drugs had already been consumed in historic populations. This investigation was done on historic skeletal remnants, either from pre-Columbian Peru or ancient Egypt. Skeletal tissue was of primary choice, as the skeletal material usually is quite resistant to postmortal autolysis. In this material, significant concentrations have been found of tetrahydrocannabinol, cocaine and nicotine [5, 6], as well as for caffeine [8]. The specificity of these measurements was evidenced by the selective presence of nicotine in skeletal material from skeletons from Middle Europe, while other drugs were absent [6].

In the present report, we describe the drug findings in an Egyptian mummy which had been unwrapped during the Munich Mummy Project [9]. These observations shed some significant light on historic medicine.

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Materials and methods

Description of the mummy

The mummy presented in this report had been transferred to the Royal Bavarian Academy of Science in the 1820s by Dr. F. W. Sieber, a private scientist from Prague (Czechia). According to ^{14}C-dating analysis the mummy has been dated back to the 21st Egyptian dynasty (approx. 950 B.C.), although the exact source of the mummy has not been determined. A more detailed report on the mummy will be given elsewhere.

During the unwrapping of the mummy which was performed due to the poor state of conservation (Fig. 1), the chest cavity revealed several small packages containing mummified organs which had been dried and then carefully wrapped in separate linen bindings. In four such packages small divine figurines were present. These represented the four sons of Horus which had also previously been found by SMITH and DAWSON [10] in lung, liver, stomach and intestine, so that an attribution of the packages to these organs could be performed (see Fig. 2). In addition, a macromorphological analysis of the organ remnants supported the aforementioned organ diagnoses, which were furthermore confirmed by histological analysis.

Analysis of drug concentrations

In an attempt to analyze both the presence and the concentrations of various drugs and/or drug metabolites, hair, skin, bone, tendon, lung, liver, stomach and intestinal tis-

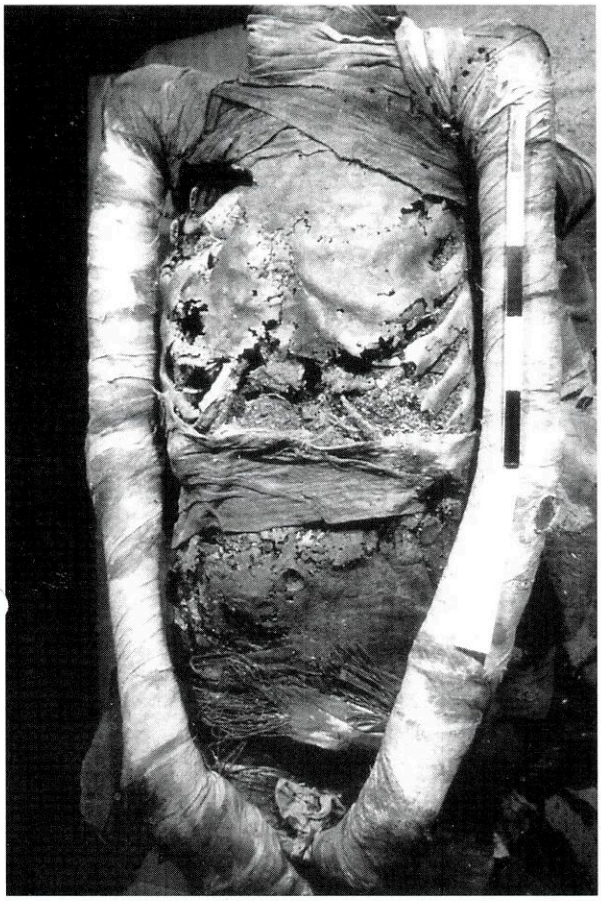

Fig. 1. Macroscopic aspect of the mummy during the unwrapping procedure, showing considerable destruction of the anterior chest wall

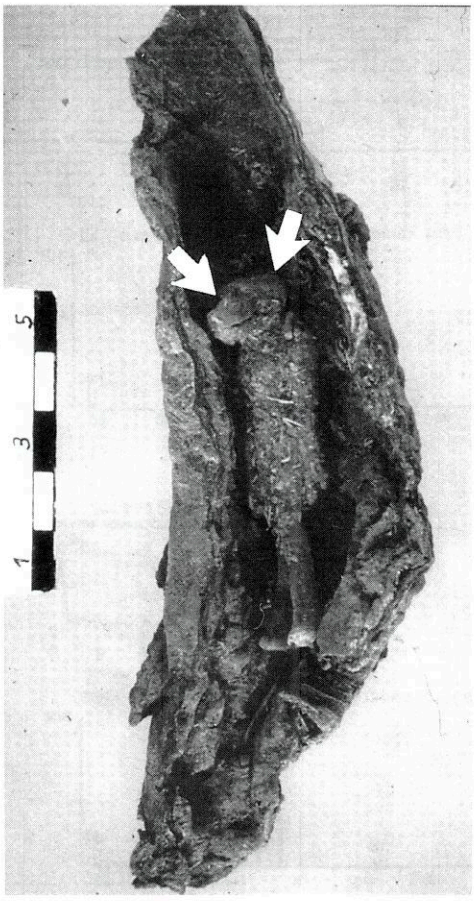

Fig. 2. Macroscopic findings of one of the organ packages. In the mummified tissue a small wax figurine representing the Horus son HAPI can be seen *(arrows)*

sue samples from the mummy were used. Thus, Δ^9-tetrahydrocannabinol (THC), nicotine and cocaine alkaloids and/or their metabolites (as the nicotine metabolite cotinine) were analyzed.

The determination of the drug concentrations was performed using specific radio immunoassay systems (Biermann Diagnostics, Bad Nauheim, FRG) and the results were confirmed by gas chromatography and mass spectrometry. All these techniques had previously been adapted to historic tissue samples [5, 6]. Briefly, the following procedure was applied: The hair samples were washed for 2 min with 10 ml distilled water and 10 ml ethanol for three times, then pulverized using a steel ball at –180° C. 50 mg were then incubated with 1 ml of 0.1 mol/l HCl overnight at 50° C. The acid extracts were alkalized (pH 9.5), extracted with chloroform, evaporized and then redissolved in phosphate buffer (pH 7.4). The samples of soft tissue, bone and teeth were washed, pulverized and then 200 mg dissolved in 0.9% NaCl. After alkalization (pH 9.5), the eluate was extracted with chloroform, evaporated and redissolved in phosphate buffer (pH 7.4) as well. The concentrations of cocaine, nicotine and THC were measured by radio immunoassay as routinely performed. The lower limits of detection were 6 ng/ml for cocaine, 12.5 ng/ml for nicotine and 5 ng/ml for THC. Amounts greater than 15 ng/ml were interpreted as positive results. The values were converted to nanogram equivalents /ml by use of a calibration curve and then converted to nanograms per gram hair or tissue, respectively. In previous experiments the intra- and interassay coefficients of variation were: cocaine 7.5% (n = 7) and 8.5% (n = 28), nicotine 6.9% (n = 8) and 7.3% (n = 31), THC 8.2% (n = 7) and 9.7% (n = 28).

For the drug determination by gas chromatography/mass spectrometry the above indicated eluates were redissolved at pH 9.5 with chloroform and restricted under nitrogen. 2 µl were injected into a GC/MS (Hewlett-Packard GC 5890, MSD 5972). The lower limits of detection were 1 ng/ml for each drug. All values were attributed by use of the recommended database library (Database Wiley L) according to the manufacturer's recommendations. In this way a concise separation of the drugs and metabolites analyzed was possible [5, 6]. In addition, previous analyses using authentic cotinine had shown a distinct separation from nicotine [2].

Histomorphological examination

For this analysis, we removed several tissue samples from each organ package and a sample from the mummy's skin

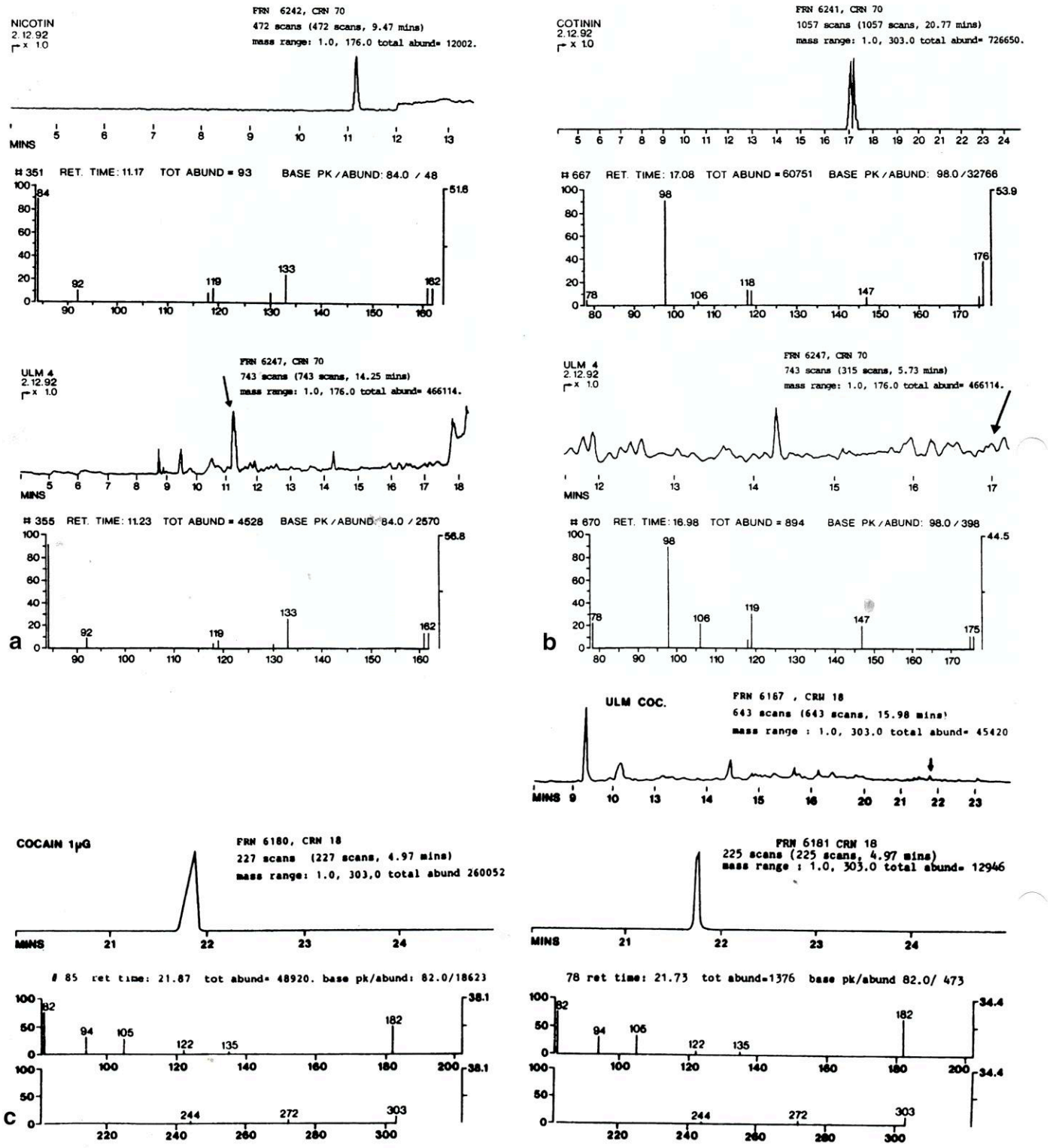

Fig. 3 a–c. GC/MS-findings in stomach tissue from the mummy: The profiles for nicotine (**a**), cotinine (**b**) and cocaine (**c**) are presented showing the respective gas chromatograms and the corresponding mass spectrometric findings. Note the standard curves at the *upper* (**a, b**) or *left* (**c**) half of the respective figures

and rehydrated them according to previous protocols [11]. The rehydrated material was then fixed in buffered 4–6% formaldehyde, embedded into paraffin and used for the preparation of tissue sections as routinely performed. In addition to the HE (hematoxiline-eosin) staining we performed several histochemical stainings, in particular connective tissue stainings (elastica-van Gieson) and the Prussian blue-reaction for the detection of iron deposits.

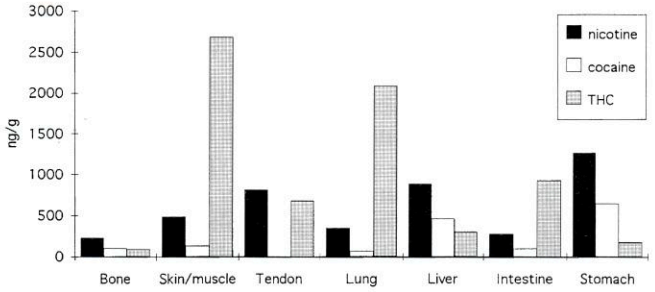

Fig. 4. The concentrations obtained for the three drugs analyzed in the different tissues

Results

Drug analysis

By use of our analytical procedure, we were able to detect significant concentrations of all drugs tested in our historic tissue samples (Fig. 3). Nicotine, cocaine and THC and/or their metabolites were present in significant amounts in hair, skin, bone, tendon, liver, lung, stomach and intestines. All values obtained for the immunoassay were confirmed by the GC/MS analysis (see Fig. 3). The levels for these drugs were consistent with those of recent drug consumers. In addition, in tissue samples we observed a certain "organotropism" of the drug concentrations: The highest levels for nicotine and cocaine were found in the stomach, whilst significant amounts of THC were located in the lung tissue, as well as in skin/muscle. Significant, but lower levels for nicotine and cocaine were seen in liver tissue. The detailed data are shown in Fig. 4. This maximum distribution points to an oral ingestion of nicotine and cocaine containing drugs, and to a preferential inhalation of THC.

Morphological analysis

The histological analysis fully confirmed the macroscopic organ diagnoses (Fig. 5). In this respect, the lung parenchyma was of particular interest: Although condensed, it was clearly identifiable. In addition, we observed here extensive disseminated deposits of a brown grainy pigmented material that was histochemically identified as large amounts of hemosiderin as evidenced by a positive Prussian blue histochemical staining (Fig. 5b). Furthermore, we occasionally found a dark anthracotic pigment in the parenchyma as well as fine particulate conglomerates of silica particles. In addition, we occasionally observed in the lung parenchyma small round calcified particles which were surrounded by a PAS-positive cuticu-

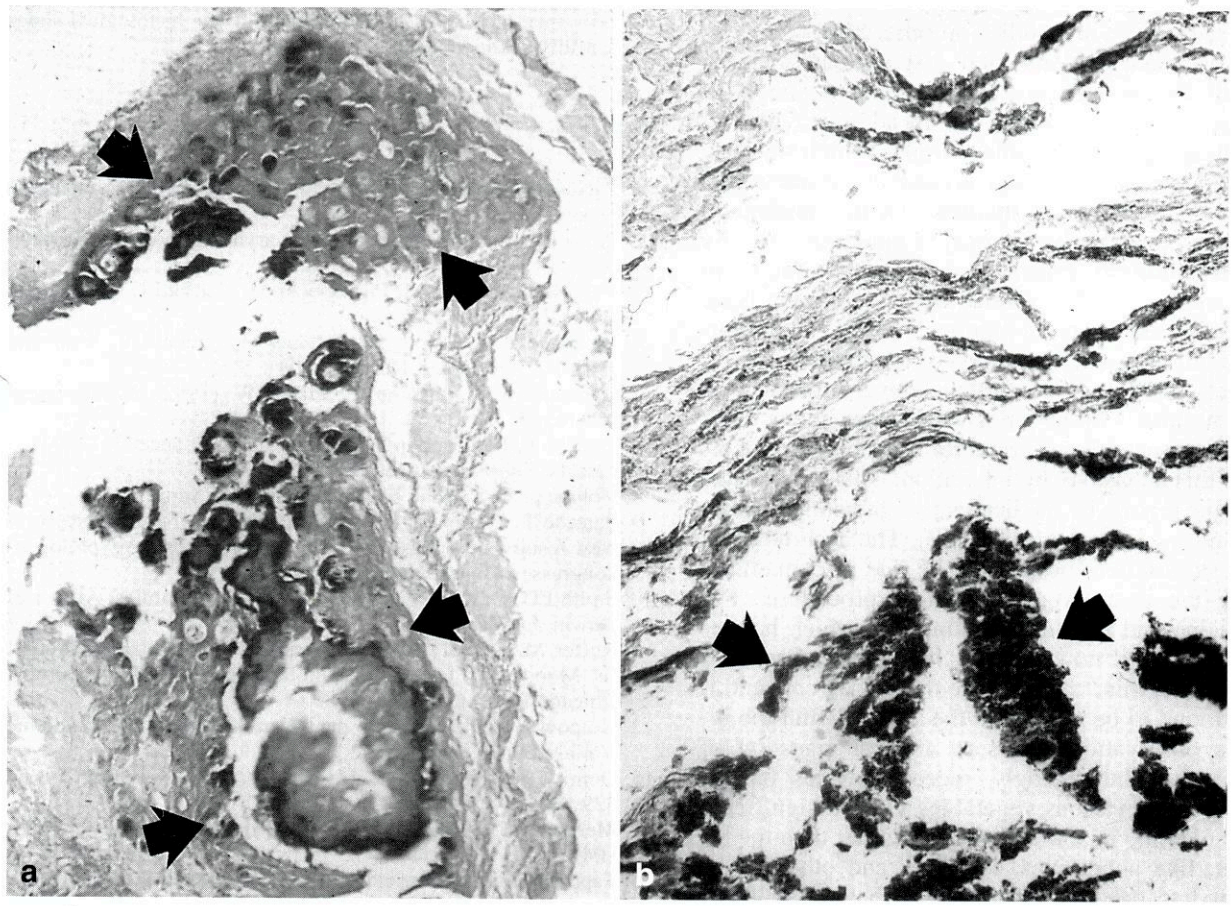

Fig. 5a, b. Histomorphological aspects of the mummy's lung tissue. (**a**) The typical features of partly calcified bronchial cartilage residues *(arrows)* in the tissue sample clearly indicate the presence of lung tissue. (**b**) Within the collapsed alveoli of the lung parenchyma focal deposits of hemosiderin can be found *(arrows)*. (**a**: HE × 400; **b**: Prussian blue × 300)

lum-like material most presumably representing remnants of parasitic infiltrates.

The additional histological analysis of the other organs showed typical structures of liver tissue (without any evidence for fibrotic tissue reaction), structures of the intestines and the stomach. In all these organs no major pathological findings could be noted. (A detailed report of the histopathological observations will be presented elsewhere).

Discussion

The major finding was that the drugs (and some of their metabolites) could cleary be identified in the tissue samples analyzed, indicating that these substances are stable over an unexpectedly long period of time. This fact may – at least in part – be due to the cyclic molecular structure of the substances tested. In addition to previous reports [5–8], we observed that significant amounts of various drugs were present in several different tissues. Although the absolute values of the drug concentrations may show considerable interbatch variation [8] – in particular when tested by the immunoassay system –, the intrabatch analysis, as in this study, reflects correct relative proportions. Thus, our analysis of the concentrations of various drugs in different mummy tissues sheds some light on historic therapeutic measures. The specificity of these findings is corroborated by previous studies on other historic material. Thus, we have demonstrated that skeletal material from Middle Europe selectively contained nicotine, but not the other substances tested [6]. In addition, the evidence for the nicotine metabolite cotinine, which was also found in the present material, argues in favour of an intravital consumption of nicotine (with subsequent metabolization) rather than simply a contamination by nicotine post mortem. Furthermore, these findings are well in accordance with previous observations on bone samples from other Egyptian mummies [5, 8]. The observation of significant concentrations of tetrahydrocannabinol – which represents the psychoactive substance of drugs as in hashish – in the lungs with values above those of the other internal organs, argue for a preferential incorporation of this substance by inhalation. This is in accordance with the reports by medical papyri indicating smoking ceremonies, e.g. with hashish [12]. The accumulation of THC in skin/muscle tissue may be due to contamination during the postmortal embalming procedure. The way of cocaine and nicotine consumption which has remained unclear until now [7] may have been uncovered by the analysis of this "case": Since these drug concentrations were found to be highest in the stomach and the intestine, this observation points to an oral ingestion of these substances. Interestingly, recent analyses on the nicotine content of various vegetables yielded significant amounts of nicotine in some plants [13] other than the tobacco plant, like aubergines, tomatoes and others. Furthermore, it has recently been shown that in Southern Africa a nicotine containing plant (Nicotiana Africana) occurs [14], which may have been accessible to ancient Egyptians. Thus, the use of these substances as therapeutic drugs may have had a firm place in the old Egyptian medicals' repertoire.

In addition to the biochemical observations on the drugs in the different mummy tissues, we observed some pathological alterations which may hypothetically be related to the drug consumption. In our present study, we observed pathological findings particularly in the lung tissue. Besides the deposition of large amounts of birefringent silicate – as it has been shown both in other mummies [15] as well as in recent populations in desert areas [16, 17] and which are presumably caused by the inhalation of sand dust during desert storms – we found an extensive intravital bleeding into the lung tissue, particularly into the small alveolar air spaces. As the possible cause for these bleedings we provided some evidence that our individual suffered from a parasitosis which manifested in the lungs.

According to these observations, it seems reasonable to speculate that our "historic patient" suffered from a pulmonary parasitosis which led to a (recurrent?) intravital pulmonary bleeding. It may thus be speculated that the extensive pulmonary haemorrhage – probably due to the parasitosis – significantly contributed to the final lethal course of the patient.

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