

ABSTRACT

The Ancient Nubians (A.D. 350) have historically been renowned for their significant contributions to medicine. In spite of this, extremely poor oral health plagued this population. Paleopathological studies depict pronounced dental deterioration patterns far exceeding normal physiological progression. The advanced wear is popularly attributed to sand particle contamination of their daily diets. However, considering that individual wear mechanisms rarely act in isolation, we propose that adverse biochemical factors arising from regular consumption of tetracycline-fortified beer induced calcium malabsorption, and thus provided a synergistic diathesis in potentiating these effects.

We examine these implications within the context of prevalent therapeutic remedies, bone fluorescence labeling data, and sociocultural attitudes when making the link between tetracycline and the compromised integrity of teeth, while citing the emergence of antibiotics actually predating formally-accepted convention.

BACKGROUND

Dental Paleopathology

Largely due to ancient Egypt's arid climate and elaborate burial customs, paleopathologists and anthropologists alike have benefited from well-preserved mummified and skeletal remains to offer insight into health patterns prevalent among this civilization. Based on vast archaeological and ethnographic evidence, dental disease was particularly pronounced, most of which have been attributed to excessive tooth wear to the extent of pulpal exposure, and consequently apical infection¹. Upon further analysis, key dentition trends emerged, implicating dietary sources contaminated with inorganic particles, thereby forming the premise for the sand theory².



Figure 1: Egyptian Skull c. 1,500 BC
Credit: R. Forshaw²

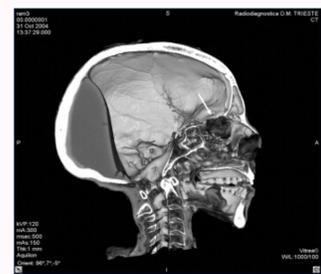


Figure 2: Dental Trauma denoted by Heavy Occlusal Wear
Credit: M. Cook et al³

Tetracycline Fermentation

Although the ancient population shifted from hunter-gatherers to agriculturists depending on the availability of food sources, bread and beer were staples³. Provided by wheat, barley, and millet⁴, the two were inextricably-linked. In the predominant method of brewing, dough captured airborne yeast before being partially baked, allowing for the yeast to grow in an optimal environment. This was then broken and added to a malted grain broth, subsequently fortified with streptomycetes commonly extracted from soil. Given the extreme conditions to which the bacteria were subjected, their tetracycline yield was maximized, giving rise to what was revered as medicinal beer⁵. Attuned to its nutritional and therapeutic viability, studies indicate that the ancient Egyptians regularly and intentionally consumed beer not only as a remedy, but as an antibiotic prophylaxis⁶.

HYPOTHESIS

Given that tooth wear mechanisms generally act synergistically, it is proposed that tetracycline chelation compounded the loss of enamel and dentine degradation of teeth, thereby advancing the onset of common disease manifestations endemic to the ancient Egyptians.

THEORY

Mechanism of Action

Tetracyclines exhibit broad-spectrum bacteriostatic activity, particularly effective against gram-positive and gram-negative bacteria. By binding to a bacterium's 30S ribosomal subunit to block aminoacyl-tRNA's binding to the mRNA acceptor site, the addition of amino acids in a developing peptide chain is prevented, thereby halting protein synthesis⁷.

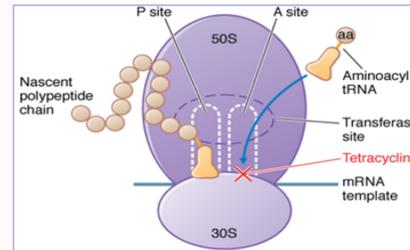


Figure 3: Tetracycline's Inhibitory Mechanism
Credit: Basic Medical Key⁷

Furthermore, tetracycline acts as a chelating agent that breaks intermolecular bonds within dental tissues and forms complexes with divalent or trivalent metal cations, resulting in insoluble and inabsorbable compounds subsequently excreted in urine.

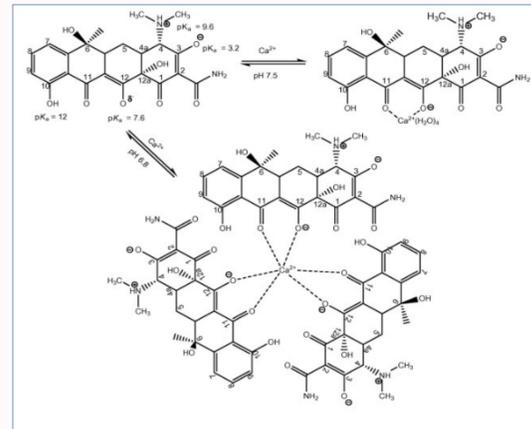


Figure 4: Potential Routes of Tetracycline-Calcium Complexation

Tetracycline's intrinsic ability to form drug-metal complexes not only drives their antibacterial action, but draws the linkage between calcium depletion and its consumption. Since the essential mineral is critical in maintaining the integrity of bones and teeth, its deficiency leaves these structures especially susceptible to alternative wear mechanisms.

MATERIALS AND METHODS

Bone Fluorescence Labeling

At physiological pH, tetracycline's affinity for calcium ions causes it to become incorporated as tetracycline-calcium orthophosphate complexes in mineralizing tissues. Under ultraviolet microscopy excitation, bone specimens from the ancient Egyptian population containing tetracycline would theoretically induce a yellow-green fluorescence that conform to osteonal patterns identical to the findings produced in comparative contemporary analyses⁸. Given that exposure is relative to the quantity of labeled osteons, and thus width of band deposition, whether tetracycline was consumed, as well as insights into dosage and frequency patterns, can be interpreted.

Mass Spectroscopic Characterization

To refute claims that any identified fluorescence resulted from postmortem bacterial infiltration as opposed to antemortem tetracycline ingestion, a more substantive means of analysis presented by mass spectroscopy should be engaged. Samples exhibiting fluorescence can be demineralized using hydrogen fluoride to dissolve calcium-tetracycline complexes, then isolated by solid phase extraction, and finally characterized by high pressure liquid chromatography⁹. These results can then be compared to an experimental control, known tetracycline compounds, under the same conditions in vitro.

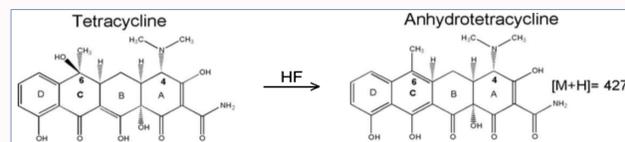


Figure 5: Chemical Conversion of Tetracycline to Anhydrotetracycline during HF Acid Demineralization of Bone
([M + H]⁺ is the molecular weight of the product plus hydrogen sought after in mass spectral data)
Credit: M. Nelson et al⁹

DATA & DISCUSSION

Bone Fluorescence Labeling

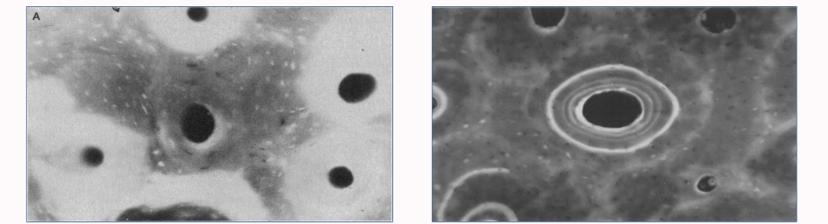


Figure 6: Osteon Sample from Ancient Egyptian Adult, dosage unknown
Credit: E. Bassett et al⁴

Figure 7: Differential Tetracycline Labeling in Modern Adult, interval dosage
Credit: M. Cook et al³

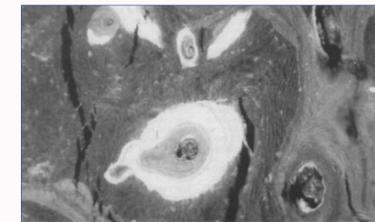


Figure 8: Differential Tetracycline Labeling in Modern Adult, continuous dosage
Credit: M. Cook et al³

On a qualitative basis, the first and third images (Figures 6 and 8) exhibit identical fluorescence data; this corroborates the detection of tetracycline in the sample. With regards to dosage, the amplified, thick concentric rings (Figure 6) are analogous to those in the referential standard imaging of tetracycline administered continuously (Figure 8).

Mass Spectroscopic Characterization

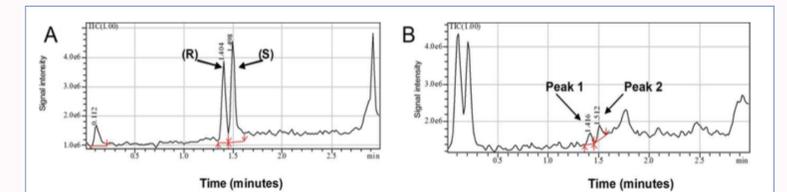


Figure 9: Total Ion Chromatogram
Retention times of anhydrotetracycline and their mass spectra, [M + H]⁺ = 427.1 amu (A) and ancient bone specimen and corresponding mass spectra [M + H]⁺ = 427.1 amu (B).
Credit: M. Nelson et al⁹

Mass spectroscopic characterization findings validate the labeled bone and eluting extraction bands as the chemically-modified derivative anhydrotetracycline. Given both the identical retention times of the chromatograph peaks and mass spectra data derived from the sample, the presence of tetracycline is confirmed, and at considerable levels.

CONCLUSION

In conclusion, the ancient Egyptians' chronic consumption of tetracycline-infused beer likely acted as a causal factor impacting their dental health as gauged by both parameters of physical abrasion and chemical corrosion. The chelating property of these antibiotics function to demineralize tooth enamel, thus altering the microenvironment surrounding dental tissues, while decreasing the bioavailability of calcium. This renders teeth increasingly vulnerable to attrition, resulting from the cumulative effects of both physical abrasion from inorganic particles and exposure to antagonistic biochemical agents.

Furthermore, a justified hypothesis can be drawn that this civilization can be credited with the discovery of tetracycline – a theory that contradicts modern perspectives attributing its discovery to Benjamin Duggar in 1945¹⁰. In this pre-antibiotic era, fortified brews were leveraged pharmacologically to treat a variety of ailments, as evidenced by low rates of infectious disease¹¹. Despite relatively good systemic health, adverse consequences of chelation promoted notoriously declining dental morphology.

REFERENCES

- Forshaw R.J. "The Practice of Dentistry in Ancient Egypt." *British Dental Journal*. Volume 206, No. 9, May 9 2009.
- Forshaw R. "Dental Indicators of Ancient Dietary Patterns: Dental Analysis in Archaeology." *British Dental Journal*. Volume 206, No. 9, May 9 2014.
- Forshaw R.J. "Dental Health and Disease in Ancient Egypt." *British Dental Journal*. Volume 208, No. 8, April 25 2009.
- Bassett E.J, Keith M.S, Armelagos G.J, Martin D.L, and Villaneuva A.R. "Tetracycline-Labeled Human Bone from Ancient Sudanese Nubia (A.D. 350)." *Science* 209, No. 4464.
- Armelagos, George J. "Take Two Beers and Call me in 1,600 Years." *Natural History*. Volume 109, Issue 4, May 2000.
- Cook Megan, Mollo El, and Anderson C. "Fluorochrome Labelling in Roman Period Skeletons from Dakkheh Oasis, Egypt." *American Journal of Physical Anthropology*. 80, (1989).
- Chepran Ian and Roberts Marilyn. "Tetracycline Antibiotics: Mode of Action, Applications, Molecular Biology, and Epidemiology of Bacterial Resistance." *Microbiology and Molecular Biology Reviews*. June 2001.
- Nelson Mark, Dinardo Andrew, Hochberg Jeffrey, Armelagos George. "Brief Communication: Mass Spectroscopic Characterization of Tetracycline in the Skeletal Remains of an Ancient Population from Sudanese Nubia 350-550 CE." *American Journal of Physical Anthropology*. 143, (2010).
- Aminov, Rustam. "History of Antimicrobial Drug Discovery: Major Classes and Health Impact." *Biochemical Pharmacology*. 133, (2017).
- Hummert James R and Van Gerven, Dennis P. "Tetracycline-Labeled Human Bone from a Medieval Population in Nubia's Batn El Hajjar (550-1450 A.D.)." *Human Biology*. May 1982.
- "Protein Synthesis Inhibitors and Miscellaneous Antibacterial Agents." *Basic Medical Key*. <<https://basicmedicalkey.com/protein-synthesis-inhibitors-and-miscellaneous-antibacterial-agents-2/>>