J. Clin. Chem. Clin. Biochem.

Vol. 25, 1987, pp. 719–722

© 1987 Walter de Gruyter & Co.
Berlin · New York

Renal Stone Analysis:

LITHOS, an Expert System for Evaluation of X-Ray Diffractograms of Urinary Calculi

By *R. W. Wulkan, L. Zwang, T. L. Liem, B. G. Blijenberg and B. Leijnse*

*Department of Clinical Chemistry, Academic Hospital Rotterdam-Dijkzigt and
Department of Chemical Pathology, Erasmus University Rotterdam, The Netherlands*

(Received May 14/July 4, 1987)

Summary: An expert system for evaluation of X-ray diffraction patterns of urinary calculi is described and evaluated. The software was developed using the PERSONAL CONSULTANT expert system shell from Texas Instruments.

Introduction

X-ray diffraction as a technique for analysis of urinary stones has a history of 16 years in our laboratory (1, 2), and in the recent past has been shown to perform well in both Dutch and German surveys (3).

The analysis requires a considerable amount of skill and experience, which cannot easily be transferred to other personnel. Furthermore, the introduction of a shock wave lithotripter into our hospital has confronted us with a twofold increase in workload, amounting to a total of 2100 stones last year. In order to permit on line processing of diffraction data, an X-ray diffractometer operated by a personal computer was recently introduced in our laboratory. Thus provided with the necessary hardware, we decided, for the reasons mentioned above, to apply our knowledge to an expert system.

Materials and Methods

The diffractometer

The diffraction analysis makes use of a Compact X-ray Diffraction Analyser System 1840/10 from Philips, Eindhoven, The Netherlands. Briefly, this system consists of a goniometer driven by a stepper motor, a solid state detector, a high voltage generator, an X-ray tube, a strip chart recorder and a control unit. The latter is equipped with an integrator/interface board which permits remote control by means of a personal computer.

Hardware

The analytical data, i.e. diffraction angles (theta values) and integrated intensities of the reflections are sent to an Olivetti M24 Personal Computer (PC) equipped with a 10 Mb Winchester drive and one floppy drive. The PC has an extended internal memory of 640 Kb and a 8087 coprocessor unit.

Software

A demonstration program written in GW-BASIC for remote controlled operation was supplied by the manufacturer. The program was extended to facilitate data handling by adding the following features:

1. Storage of primary data
2. Baseline correction
3. Peak selection
4. Storage of selected data in a LISP format

The expert system was developed using the Personal Consultant (TM) shell from Texas Instruments, Austin, Texas, USA. Additional use was made of IQLISP version 1.7, also from Texas Instruments.

Standards

Standards of human material were prepared for whewellite, weddellite, apatite, struvite, brushite, whitlockite, uric acid, and uric acid dihydrate from stones judged to be pure components by the *Debye-Scherrer* technique. We avoided using commercially available material because in preliminary experiments we observed some differences in diffraction properties with human material.

Magnesium oxide was obtained from E. Merck, Darmstadt, F. R. G.

Sample preparation

Samples are prepared by grinding the stones in an agate mortar and layering the resulting powder (5 mg minimally) on a monocrystalline disk of silicon (Philips, PW 1817/32). This applicator has the advantages of a low background and absence of interfering peaks. The disk is then manually placed in a fixed position in the measuring chamber of the diffractometer. The sample is scanned over a range of 4.5 to 22.5 degrees of theta in a time interval of 12 minutes.

The PERSONAL CONSULTANT expert system shell

The PERSONAL CONSULTANT shell provides a development environment for building expert systems. It is written in LISP, one of the languages traditionally used in artificial intelligence. The shell can be „filled“ with rules representing the knowledge of the human expert. Each rule consists of a premise and an action, both written in a sort of pseudocode to facilitate the use to those who are not familiar with LISP. When during consultation a certain rule is checked, the action is carried out only if the premise is true. Additional tasks can be carried out by LISP functions contained in the premise or action.

The rules are grouped in several functional domains called contexts, each representing a specific part of the knowledge. One of the advantages of this approach is a gain in time, because only those rules that are relevant to the actual situation are checked. The system is goal-driven, i. e. during consultation all rules with a so-called goal parameter in their action are retrieved, then their premises are verified one by one, which in turn leads to retrieval of other parameters and rules and so on. When all such goals are established the consultation is ended and results may be printed or stored on disk. For a more detailed description of comparable systems the reader is referred to the literature (4).

LITHOS

The expert system has been designed to serve one main purpose, i. e. qualitative and semi-quantitative determination of the composition of the stone.

At present the system contains 52 rules which are grouped in a parent context that is allocated during each consultation, and 11 subcontexts which deal with specific difficulties. The parent context handles general tasks such as the production of a first matched list, the calculation of the relative contents of the components and the generation of a report, which will be described hereafter.

To determine the composition of the sample, LITHOS requires a set of theta values and matching intensities. These can be entered either from the keyboard or from a disk file that has been created by the BASIC program described above. The number of combinations (thetas and intensities) for input to the system can be freely chosen and in practice will be limited to 1–15 combinations, but values as great as 50 are allowed.

The expert system contains in its knowledge base the names of the components it is able to detect, each with a set of theta values that have been found for the pure component. The first theta value to follow the component name is always found when the component is present. During consultation the system compares the input theta values and associated component names and produces a list of matched theta values and associated component names.

Because the theta values show a slight run-to-run variation we have permitted the matching process to take place within a small margin. In this way the system will not miss important

theta values, even if the last decimal shows a small variation. Components without the presence of their specific theta value are omitted from this list. This is a first safety measure to prevent the system from presenting artifactual results.

Other artifacts may be present, e.g. an observed theta value due to the presence of component A may coincide with the specific theta value of component B which is absent from the sample. This situation, which occurs especially with samples containing amorphous components e.g. apatite, is solved by a special set of rules (subcontext) that is allocated only when A and B are present in the first matched list. From the intensity ratio of the theta value shared by A and B and a second theta value of A, the absence or presence of component B is concluded. In the former case, component B is removed from the list of selected components. In the latter case the intensity of the B-specific theta is corrected for the contribution of A. These rules act as a second safety measure to prevent artifacts.

In order to prevent the system from doing the unnecessary work of checking the rules in a subcontext when the pair of components A/B is not present, LITHOS contains a metarule that decides which subcontexts are to be entered and which subcontexts are irrelevant to the actual situation.

The latter will vary with each new consultation, and therefore we have provided the system with a LISP function that alters the metarule during each consultation according to the needs of the moment. After all the necessary subcontexts have been consulted a final list of authorised components is produced.

We have experienced that maximally four components are found and therefore we have limited the number of components that can be determined to five.

The next step in the consultation is the determination of the relative content of each component in the sample. In order to correct for differences in mass absorption coefficient for the various components, the internal standard technique as described by *Rebentisch & Berg* (5) is applied. These authors determined the intensity ratios of the various pure components relative to magnesium oxide and used these to correct for the differences in mass absorption coefficient. These ratios are incorporated in the knowledge base and are used to calculate the percentual content for each component.

Finally, a report is generated on the screen containing the patient name, the time of day, the date, and the list of components and their relative content. This can then be printed or stored on disk.

Another option of LITHOS when running in the interactive mode is that of an electronic encyclopaedia in its field of knowledge. The user may select from a menu of items to get a page-by-page display of the information stored in corresponding disk files. Paging backwards is allowed as well as interrupting to process at any moment, after which a return to the menu for a new selection is offered. All kinds of information can be stored and added in a process of continuous growth, e.g. chemical, physical, morphological and epidemiological data about the various components, dietary information, data about pharmaceutical therapy etc.

Results

Accuracy and precision

The day-to-day variation was evaluated by analysing five different mixtures of pure human standards each day over a period of ten days. The results are presented in table 1.

Tab. 1. Evaluation of accuracy and precision of the diffractometer method including LITHOS. The third column gives the composition (g/kg) as prepared from human standards, the fourth column gives the mean content of ten analyses, the last column gives the standard deviation.

No.	Components	Prepared composition (g/kg)	Mean composition of 10 analyses (g/kg)	Standard deviation (g/kg)
1.	Struvite	370	400	20
	Whewellite	290	300	20
	Weddelite	210	190	30
	Apatite	130	100	20
2.	Struvite	570	560	50
	Weddelite	390	420	30
	Whewellite	40	20	50
3.	Uric Acid	490	430	20
	Whewellite	490	530	30
	Weddelite	20	20 ¹⁾	10
4.	Uric acid · 2 H ₂ O	670	590	30
	Brushite	260	370	40
	Whewellite	70	20 ²⁾	20
5.	Uric acid	330	220	30
	Apatite	290	280	60
	Weddelite	340	450	60
	Whewellite	40	50	20

¹⁾ An extra (mean) 30 g/kg of apatite was found

²⁾ An extra (mean) 4 g/kg of weddelite and 7 g/kg of sodium urate was found

Tab. 2. Results of the *Debye-Scherrer-Hull* method and the diffractometer method including the expert system by analysis of twenty human calculi. Analytical data are given in g/kg by the former and the latter method, respectively.

<i>Debye-Scherrer-Hull</i> method/Diffractometer + LITHOS					
Apatite (g/kg)	Brushite (g/kg)	Struvite (g/kg)	Weddelite (g/kg)	Whewellite (g/kg)	Whitlockite (g/kg)
				1000/1000	
	1000/1000				
1000/950			-/50		
			-/90	1000/910	
900/720				100/280	
	600/530				400/470
900/860				100/140	
200/110				800/890	
700/730		300/270			
	1000/950		-/50		
trace/40			1000/910	trace/50	
200/230			800/730	-/30	
trace/-			600/640	400/360	
600/510			300/360	100/130	
300/350	trace/70				700/580
100/110			900/890	trace/-	
100/150			500/500	400/350	
-/40			-/60	1000/900	
100/160		900/770	-/70		
600/570			-/30	400/400	

For reasons mentioned earlier (see standards) the method was evaluated by comparison with the results obtained with the *Debye-Scherrer-Hull* technique. The results of twenty analyses of patient calculi are given in table 2.

The results in table 2 were evaluated by orthogonal regression for apatite, weddelite for whewellite, and for the major component in each sample (tab. 3).

Discussion

X-ray analysis of renal stones is a technique which, even in our time of sophisticated analytical chemistry, presents us with many problems such as relatively low precision and choice of appropriate standards. Although, together with infrared analysis, it is the method of choice for the analysis of human calculi, as a rule the results are only correct within 10% (6). Furthermore the skill required is only gathered during years of analytical experience. These factors, together with the well defined nature of the expertise makes it an excellent field of knowledge for the development of an expert system.

Tab. 3. Statistical evaluation of data given in table 2. For three components, the results of the diffractometer method including expert system were compared to those of the *Debye-Scherrer-Hull* method by means of orthogonal regression analysis. The last column gives the data when the content of the major component is compared as analysed by either method. The intercept is given in g/kg.

	Apatite	Weddelite	Whewellite	Major Component
Correlation	0.98	0.996	0.98	0.93
Intercept (g/kg)	30	60	50	-30
Slope	0.89	0.88	0.91	0.98
Standard deviation a	0.04	0.02	0.06	0.09
Standard deviation b	27	12	35	77
Number of analyses	13	12	11	20

The implementation of LITHOS took approximately one year and in this period we experienced how the development of an expert system compels one to make explicit even the most remote parts of the expertise.

As can be seen from tables one to three, the combination of the diffractometer with an expert system performs well in terms of modern standards of analytical performance in this field, both in accuracy and precision as well as in comparison with the traditional *Debye-Sherrer-Hull* method. These figures present only a preliminary evaluation. Results with an in-

creased number of components will be subsequently published, together with a discussion of artifacts and problems of standardisation.

Acknowledgement

We want to express our thanks to Mrs. *A. P. Copper-Staamer* for her fast and accurate typing.

References

1. Boer, N. C. den, Bakker, N. J. & Leijnse, B. (1972) Ned. Tijdschr. Geneesk. 116, 373–377.
2. Blijenberg, B. G., Liem, T. L. & Leijnse, B. (1986) Ned. Tijdschr. Geneesk. 130, 354–356.
3. Röhle, G., Voigt, U., Hesse, A. & Breuer, H. (1982) J. Clin. Chem. Clin. Biochem. 20, 851–859.
4. Shortliffe, E. H. (1976) MYCIN. Amsterdam: Elsevier/North-Holland Inc.
5. Rebentisch, G. & Berg, W. (1983) J. Clin. Chem. Clin. Biochem. 21, 665–671.
6. Otnes, B. & Montgomery, O. (1980) Investigative Urology 17, 314–319.

R. W. Wulkan
Department of Clinical Chemistry
Academic Hospital Rotterdam-Dijkzigt
Dr. Molewaterplein 40
NL-3015 GD Rotterdam