A FAST COMPARISON OF IR-SPECTRA FOR SCREENING NEW ANTIBIOTICS

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Rapid, efficient screening of new antibiotics depends on quick determination of similarity or identity with earlier-described materials. The infra-red spectrum contains a wealth of specific information and comparison of spectra should be a useful tool at an early stage of investigation. However, there are several difficulties with using all the information in the IR spectrum. If peak position only is used, there is considerable confusion between compounds with similar functional groups. Multiple functional groups give rise to overlap.

For maximum information the entire spectrum must be used but this causes difficulties in presenting the data. The new procedure described here is based on the concept that the position and intensity of the individual peaks relative to each other reflect the structural character of the molecule. The spectrum is divided into small portions and the character of each segment indicated by a numerical code. These codes are then used for comparison purposes either manually or by computer.

First, the IR curve from 700 cm^{-1} to 3700 cm^{-1} is divided into 15 measuring range divisions (MRD) as shown in Table 1.

Next, the character of the curve in each MRD is determined and recorded as a two digit number. The first or 10's digit represents the relative intensities of the peaks or the general shape of the curve in the MRD as shown by Table 2. The second (units) digit is the number of peaks in the MRD. Examples of code assignment are given in Figs. 1~3.

By this method the entire spectrum represented by 15 two-digit number which can be obtained from published spectra as well as experimental spectra. The evaluation and code assignment can be manual or by computer. An example of a code list from the computer is shown in Table 3.

The comparison of two antibiotics can be accomplished in the computer by coding and then adding the new code to the file after it has been compared with all the other spectra on file.

Two spectra in coded form are compared by first determining the difference in the code for each MRD. These differences (absolute values) are added to give a total which is

Table 1

MRD	cm^{-1}	micrometres
1	3700~3030	2.70~ 3.29
2	3030~2700	3.30~ 3.69
3	2700~1820	3.70~ 5.49
4	1818~1669	5.50~ 5.99
5	1667~1540	6.00~ 6.49
6	1538~1430	6.50~ 6.99
7	1429~1335	7.00~ 7.49
8	1333~1252	7.50~ 7.99
9	1250~1178	8.00~ 8.49
10	1175~1110	8.50~ 8.99
11	1111~1055	9.00~ 9.49
12	1053~1000	9.50~ 9.99
13	1000~ 910	10.00~10.99
14	910~ 800	11.00~12.49
15	800~ 700	12.50~14.50

Table 2

Type	Code
A) ascending cm^{-1}-values/ascending peak intensities	10
B) 〃 /alternating 〃	30
C) 〃 /descending 〃	50
D) 〃 /curve minimum, no peak	40

Zero in the unit-position means no peak in this MRD.

Table 3. Part of a code-list

Address	MRD													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
000 072	34	33	12	50	13	52	53	51	33	12	52	11	34	53	52
000 074	51	11	11	11	51	11	51	51	11	32	40	52	10	51	32
000 077	51	36	30	11	11	11	52	51	51	12	52	11	11	12	32
000 080	51	12	12	32	33	11	33	12	11	12	11	40	33	52	12
000 083	11	33	30	11	51	11	33	53	13	52	52	52	12	35	52

termed the curve difference sum (CDS). If the two codes for a given MRD differ by more than 21, a variation in character and number of peaks is indicated for that MRD. Such cases (code difference for single MRD> 21) are counted and the total of such cases is termed the "number of limit-exceeding differences" (NLD). These indications of variation are expressed as a quantity in which the NLD is expressed as a thousands quantity,

Table 4. Computerised data on request: comparison adriamycin and other anthracyclines.

NLD, CDS	Substance
3.125	Leukaemomycin C (identical with daunomycin)
3.145	Dihydrodaunomycin
2.145	Rubomycin C
3.126	Leukaemomycin D
1.102	Daunomycinon

Fig. 1

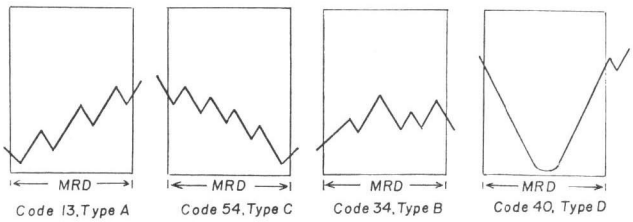


Fig. 2

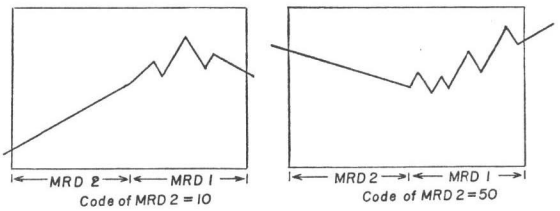
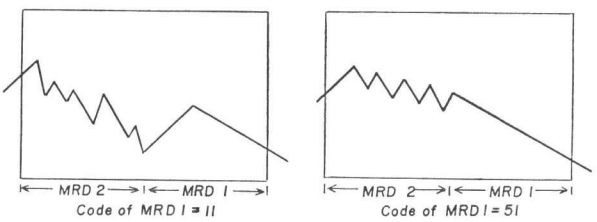


Fig. 3



followed by three digits for the CDS as shown in Table 4. The CDS and NLD values are both used in determining similarity of two spectra.

For manually evaluated curves a value of NLD not greater than 3 and CDS not greater than 150 indicates similar or identical substances. A comparison of available data gives the following results:

NLD, CDS values	Interpretation
0,000~1,150	probable identity
1,150~3,150	similarity
3,150~4,150	probable similarity
>4,150	different substances

Examples of comparison tabulations are given in next page with data from our measurements.

Values taken from the literature may be used as shown in Example 4 which compares siomycin (**I**)[3], sporangiomycin (**II**)[4] and mutabilicin (**III**)[5].

Since the original data were published FROLOVA has reported the identity of **I** and **III**[6] and of **II** and **III**[7].

Example 5 involves the following group of antibiotic: BY-81 (**IV**)[8], citromycin (**V**)[9], E-749-C (**VI**)[10], and LL-AC-541 (**VII**).[11]

Meanwhile TANIYAMA *et al.*[12] have reported

Example 1. Comparison between ir-spectra of chartreusin[1] and lambdamycin[2]

MRD	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Chartreusin	51	11	10	11	33	52	11	51	12	51	12	11	12	35	13
Lambdamycin	52	12	10	11	33	51	11	52	51	51	12	11	11	33	12
Difference	1	1	0	0	0	1	0	1	39	0	0	0	1	2	1

CDS: 45. NLD: 1. Computer written: 1.045

Example 2. Comparison between ir-spectra of lambdamycin and lambdamycinon[2]

MRD	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Lambdamycin	52	12	10	11	33	52	11	52	51	51	12	11	11	33	12
Lambdamycinon	33	13	10	52	33	33	12	53	12	52	12	11	13	34	12
Difference	19	1	0	41	0	19	1	1	39	1	0	0	2	1	0

CDS: 125. NLD: 2. Computer written; 2.125.

Example 3. Comparison between ir-spectra of chartreusin[1] and lambdamycinon[2]

MRD	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Chartreusin	51	11	10	11	33	52	11	51	12	51	12	11	12	35	13
Lambdamycinon	33	13	10	52	33	33	12	53	12	52	12	11	13	34	12
Difference	18	2	0	41	0	19	1	2	0	1	0	0	1	1	1

CDS: 87. NLD: 1. Computer written; 1.087

Example 4.

Subst.	MRD														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
I	51	12	10	51	13	32	52	50	52	53	11	11	33	12	53
II	51	11	10	51	12	33	52	51	52	53	12	11	34	12	32
III	51	12	10	51	11	32	52	52	52	53	11	12	52	12	11
I−II	0	1	0	0	1	1	0	1	0	0	1	0	1	0	21
I−III	0	0	0	1	2	0	0	2	0	0	0	1	19	0	42
II−III	0	1	0	0	1	1	0	1	0	0	1	1	18	0	21

NLD. CDS **I−II**=1.027; **I−III**=1.067; **II−III**=1.045. Conclusion: **I**, **II** and **III** are probably identical.

Example 5. IR-Comparison

Subst.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
IV	11	11	10	51	12	51	11	11	51	50	11	11	52	50	50
V	11	11	10	51	11	51	31	11	51	51	51	11	32	50	50
Diff.	0	0	0	0	1	0	20	0	0	1	40	0	20	0	0

CDS: 82. NLD. 1. NLD, CDS=1.082
Statement: Probably identical

the identity of **V** and **VII**.

From the above it can be seen that this method should be of use in the quick evaluation of related materials obtained in a screening program. It offers an objective, computer-usable method to evaluate IR curves according to the general character of the curve.

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