COMPUTER CONTROLLED SAMPLING AND ANALYSIS SYSTEM FOR DISSOLUTION RATE STUDIES

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Dissolution Rate Studies are now widely regarded as a useful, and in some cases essential, part of the quality assurance of pharmaceutical products. These studies are of a repetitive and time consuming nature and automation of the sampling and analysis is essential if a significant increase in quality assurance costs is to be avoided.

A computer controlled sampling and analysis system has been developed by ICI Pharmaceuticals Division which can be used in conjunction with commercially available dissolution apparatus meeting the requirements of the BP or USP dissolution tests. The system is applicable when the analysis is by direct UV/visible spectrophotometry and can control the sampling and analysis of one to six dissolution tests (six dosage forms per test) carried out concurrently.

The apparatus is based on a Digital Equipment Inc LSI-11 computer programmed in RTL/2 with an ICI MEDIA digital and analog input and output system. The computer requires the details of the sample type, sampling time(s) and concentration of the analytical reference solution to be used in a particular test. At each sampling time the equipment samples sequentially, via a 9 channel selector valve, a dissolution fluid blank (twice), the analytical reference solution, and each of the six sample solutions (cycle time 4 min). The absorbance of each solution is obtained by pumping 4x2 millilitre aliquots through a flow cell mounted in a single beam spectrophotometer which has variable wavelength, and variable absorbance range (CECIL CE212). The first two aliquots flush the analytical system, the third and fourth provide duplicate absorbance readings. Further aliquots are removed if the readings fail to duplicate. Variations of the cell path length (0.5 to 2mm) and absorbance units full scale (0.02 to 2.0) allows for a 400 fold change in absorbance.

Precision of the spectrophotometric readings is demonstrated by 3 consecutive sample cycles at 0.1 absorbance in a 2mm cell with the reference standard bottle and the six dissolution vessels filled with the same solution.

	ABSORBANCE									
CY	BLANK	STD	1	2	3	4	5	6	MEAN	SUCKS
1	0.003	0.104	0.105	0.105	0.105	0.106	0.105	0.106	0.105	444544
2	0.003	0.104	0.105	0.105	0.105	0.105	0.105	0.105	0.105	444444
3	0.003	0.104	0.105	0.105	0.105	0.105	0.105	0.105	0.105	444444

When the last cycle has been completed the computer calculates the percentage dissolved from each dosage at each time by comparing the nett absorbances of the sample solutions with that of the analytical reference solution. Volume changes and sample losses due to previous sample cycles are taken into account. The results are presented as a report for inclusion in batch analysis records, eg:

APPARATUS NO 1 VER NO 3 18:21:15: 10/04/79

INDERAL LA CAPSULES ADM NO 43314/79
F4042 BX UA133 STORED FOR 8 MTHS AT 37 C
FLUID 1 PH 1.5 BUFFER FLUID 2 PH 6.8 BUFFER

PERCENT DISSOLUTION OF NOMINAL DRUG CONTENT 160.0 MG

NO	TIME READ	TABLET NO 1	2	3	4	5	6	MEAN	SE
1	90	16.3	14.0	15.7	13.7	12.6	15.0	14.5	9.5
FLUID CHANGE TO PH 6.8 BUFFER									
2	300	52.3	46.2	49.6	49.7	47.1	50.6	49.3	4.6
3	480	68.0	60.6	66.2	66.3	63.1	66.8	65.2	4.2

PASSES SPECIFICATION