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Solubility of cholesterol in isopropyl myristate

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Synopsis

This report describes how the SOLUBILITY of CHOLESTEROL in ISOPROPYL MYRISTATE was determined by optical rotation. The procedure described is particularly attractive as compared to other analytical procedures used to determine cholesterol content quantitatively with respect to speed and simplicity of the measurement. The optical rotation procedure indicates that 5.26 per cent (w/w) cholesterol is soluble in isopropyl myristate.

INTRODUCTION

Cholesterol and its esters are common constituents of a number of pharmaceutical and cosmetic topical formulations (1–3). In the course of recent laboratory experiments, it was necessary to accurately determine the solubility of cholesterol in isopropyl myristate. This report describes how this was determined by optical rotation.

In addition, the procedure described herein would appear to be applicable as a general approach to the assay of optically active compounds in lipid and semisolid ingredients of the type generally used for cosmetics, toiletries, and topical pharmaceuticals.

EXPERIMENTAL

Qualitative determination of solubility of cholesterol in isopropyl myristate: Cholesterol* and isopropyl myristate† were heated to 95–100°C. The mixtures were stirred until solution was complete. The solutions were then cooled to room temperature (21°C) and observed for the presence or absence of crystals.

Quantitative determination of solubility of cholesterol in isopropyl myristate: Cholesterol and isopropyl myristate were mixed together and stored in covered beakers for at least 2 weeks. An aliquot of each solution (or an aliquot of the supernatant liquid) was withdrawn and diluted with an equivalent volume of anhydrous chloroform. Optical rotation measurements for the resulting solutions were made using the Perkin Elmer Model 141 Polarimeter‡ equipped with a 5 cc capacity, 1 decimeter cell.

RESULTS

Qualitative measurement: A series of solutions of cholesterol in isopropyl myristate were made in the concentrations as is shown in the chart that follows.

	Solution (per cent by weight)								
	A	B	C	D	E	F	G	H	I
Cholesterol	9.8	8	6	5.5	5.25	5	4.5	4	2
Isopropyl myristate	90.2	92	94	94.5	94.75	95	95.5	96	98

At t = 0, all solutions, except A and B, which were a mass of crystals, were placed at 5°C. Two and one-half hours later, solutions C, D, E, and F formed crystals and solutions G, H, and I were devoid of crystals. The mixtures were then placed at room temperature (21°C). Eighteen hours later, while at room temperature (21°C), there were no crystals in E, F, G, H, and I; C and D remained as a slurry of crystals; and A and B were almost a solid mass of crystals.

Quantitative measurement: A series of mixtures of cholesterol in isopropyl myristate was made. The system compositions ranged from 1.0 to 8.0 per cent by weight cholesterol. Table I indicates the observed rotations for all the samples made. A plot of the per cent composition versus observed rotation, at both 589 and 365 nm (as is shown in the chart that follows), over the concentration range of 1 through 5 per cent (by weight) cholesterol in isopropyl myristate was found to be linear. The rotations of the supernatants from solutions 6, 7, and 8 were used to calculate the cholesterol concentration in solution by use of the calibration curve obtained from the rotation data obtained for solutions 1 through 5 of Table I.

*U.S.P. grade supplied by Amerchol, Edison, N.J. 08817.
†Armak, Chicago, Ill. 60690.
‡Norwalk, Conn.

Per cent by weight of cholesterol in isopropyl myristate (starting mixture)	Per cent by weight of cholesterol soluble in isopropyl myristate (supernatant solution)	
	589 nm	365 nm
5.5	5.14	5.28
6.0	5.37	5.39
8.0	5.26	5.15
Average	5.26	5.27

This procedure would enable one to determine unknown cholesterol concentrations in isopropyl myristate accurately using the Perkin Elmer Model 141 Polarimeter (or equivalent) at least one order of magnitude below that reported for the lowest concentration shown in Table I. An 0.05 per cent solution of cholesterol in isopropyl myristate chloroform (1:1) has a rotation of −0.017° at 589 nm and −0.057° at 365 nm. Incidentally, at 365 nm, there is still sufficient readability of the rotation to go down to a 1 to 5 dilution.

Table I

Solution Number	Percent by Weight of Cholesterol in Isopropyl Myristate	Observed Rotation[a]	
		α_{589}	α_{365}
1	1.0	−0.163°	−0.562°
2	2.0	−0.366°	−1.217°
3	3.0	−0.540°	−1.760°
4	4.0	−0.695°	−2.382°
5	5.0	−0.868°	−2.920°
6	5.5[b]	−0.897°[c]	−3.103°[c]
7	6.0[b]	−0.938°[c]	−3.168°[c]
8	8.0[b]	−0.918°[c]	−3.028°[c]

[a]Rotation of cholesterol/isopropyl myristate solution diluted by an equivalent volume of chloroform. Readings were taken at 24°C.
[b]Crystals of cholesterol present.
[c]Supernatant solution assayed.

CONCLUSION

The estimation of cholesterol solubility in isopropyl myristate by the classical approach of visually ascertaining when the system composition can no longer support a homogeneous condition requires a large number of experiments in order to put upper and lower limits on solubility. The use of optical rotation yielded a precise solubility figure with a minimum of effort. In principal, one need only examine the supernatant of a single isopropyl myristate/cholesterol system for cholesterol content which contains solid in equilibrium with solution.

The simple optical rotation procedure indicates cholesterol is soluble in isopropyl myristate to the extent of 5.26 per cent (w/w). This technique conceivably can be

extended to include the determination of the solubility of cholesterol, cholesterol esters, and other optically active cholesterol congeners in isopropyl myristate and other optically inactive solvents. The optical rotation procedure described above is particularly attractive as compared to other analytical procedures (4) used to determine cholesterol content quantitatively with respect to speed and simplicity of the measurement.

REFERENCES

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