REFERENCES

1. Martin, A., Swarbrick, J., and Cammarata, A. in Physical Pharmacy, 3rd ed., pp. 146-147, 272-311, Lea & Febiger, Philadelphia, PA., 1983

2. Ochsner, A.B. and Sokoloski, T.D. "Prediction of Solubility in Nonideal Multicomponent Systems Using the UNIFAC Group Contribution Model" J. Pharm. Sci. 74(6), (1985) : 634-637.

3. Wu, P.L. and Martin, A. "Extended Hildebrand Solubility Approach : p-Hydroxybenzoic Acid in Mixtures of Dioxane and Water" J. Pharm. Sci. 72(6), (1983) : 587-592.

4. Martin, A., Newburger, J., and Adjei, A. "Extended Hildebrand Solubility Approach : Solubility of Theophylline in Polar Binary Solvents" J. Pharm. Sci. 69(5), (1980) : 487-491.

5. Adjei, A., Newburger, J., and Martin, A. "Extended Hildebrand Approach : Solubility of Caffeine in Dioxane-Water Mixtures" J. Pharm. Sci. 69(6), (1980) : 659-661.

6. Martin, A., Paruta, A.N., and Adjei, A. "Extended Hildebrand Solubility Approach : Methylxanthines in Mixed Solvents" J. Pharm. Sci. 70(10), (1981) : 1115-1120.

7. Williamson, A.G. in An Introduction To Non-Electrolyte Solutions, pp. 96-99, 152-161, Oliver & Boyd, Edinburgh and London, 1967.

8. Hagen, C.A. and Flynn, G.L. "Solubility of Hydrocortisone in Organic and Aqueous Media : Evidence for Regular Solution Behavior in Apolar Solvents" J. Pharm. Sci. 72(4), (1983) : 409-414.

9. Martin, A., and Carstensen, J. "Extended Solubility Approach : Solubility Parameters for Crystalline Solid Compounds" J. Pharm. Sci. 70(2), (1981) : 170-172.

10. Martin, A., and Miralles, M.J. "Extended Hildebrand Solubility Approach : Solubility of Tolbutamide, Acetohexamide, and Sulfisomidine in Binary Solvent Mixtures" J. Pharm. Sci. 71(4), (1982) : 439-442.

11. Hansen, C.M. and Beerbower, A. in Encyclopedia of Chemical Technology, Suppl. vol., 2nd ed., pp. 889-910, Wiley, New York, NY., 1971.

12. Sunwoo, C. and Eisen, H. "Solubility Parameter of Selected Sulfonamides" J. Pharm. Sci. 60(2), (1971) : 238-244.

13. Barton, A.F.M. "Solubility Parameters" Chem. Rev. 75(6), (1976) : 731, 744-746.

14. Martin, A., Wu, P.L., and Velasquez, T. "Extended Hildebrand Solubility Approach : Sulfonamides in Binary and Ternary Solvents" J. Pharm. Sci. 74(3), (1985) :277-282.

15. Ochsner, A.B., Bellato, R.J., and Sokoloski, T.D. "Prediction of Xanthine Solubilities Using Statistical Techniques" J. Pharm. Sci. 74(2) (1985) : 132-135.

16. Martin, A., Wu, P.L. Adjei. A., Lindstrom, R.E., and Elworthy, P.H. "Extended Hildebrand Solubility Approach and the Log Linear Solubility Equation" J. Pharm. Sci. 71(8), (1982) : 849-856.

17. Hansen C.M. "The Universality of the Solubility Parameter" I & EC Product Research and Development 8(1), (1969) : 1-11.

18. Beerbower, A., Wu, P.L., and Martin, A. "Expanded Solubility Parameter Approach I : Naphthalene and Benzoic Acid in Individual Solvents" J. Pharm. Sci. 73(2), (1984) : 179-188.

19. Martin A., Wu, P.L., and Beerbower, A. "Expanded Solubility Parameter Approach II : p-Hydroxybenzoic Acid and Methyl p-Hydroxybenzoate in Individual Solvents" J. Pharm. Sci. 73(2), (1984) : 188-194.

20. Wu, P.L. Beerbower, A., and Martin, A. "Extended Hansen Approach : Calculating Partial Solubility Parameters of Solid Solutes" J. Pharm. Sci. 71(11), (1982) : 1285-1287.

21. Martin, A., Wu, P.L., Adjei, A., Beerbower, A., and Prausnitz, J.M. "Extended Hansen Solubility Approach : Naphthalene in Individual Solvents" J. Pharm. Sci. 70(11), (1981) : 1260-1264.

22. Moustafa, A., Molokhia, A.M., and Gouda, M.W. "Phenobarbital Solubility in Propylene Glycol-Glycerol-Water Systems" J. Pharm. Sci 70(10), (1981) : 1172-1174.

23. Elworthy, P.H. and Worthington, H.E.C. "The Solubility of Sulphadiazine in Water-Dimethylformamide Mixtures" J. Pharm. Pharmac. 20, (1968) : 830-835.

24. Yalkowsky, S.H.,Amidon, G.L., Zografi, G., and Flynn, G.L. "Solubility of Nonelectrolytes in Polar Solvents III : Alkyl p-Aminobenzoates in Polar and Mixed Solvents" J. Pharm. Sci. 64(10), (1975) : 48-50.

25. James, K.C. and Robert, M. "The Solubilities of the Lower Testosterone Esters" J. Pharm. Pharmac. 20, (1968) : 709-714.

26. James, K.C., Chu, T.N., and Noyce, P.R. "Solubilities of Testosterone Propionate and Related Esters in Organic Solvents" J. Pharm. Sci. 65(5), (1976) : 656-659.

27. Parrott, E.L. in Pharmaceutical Technology, pp. 140, 154, Burgess Publishing Company, Mineapolis, MN.,1970.

28. Neter, J. and Wasserman, W. in Applied Linear Statistical Models, pp. 215-267, 273-293,Richard D. Irwin, Inc., Homewood, IL.,1974.

29. Nie, N.H., Hull, C.H., Jenkins, J.G., Teinbrenner, K.,and Bent, D.H. in SPSS, Statistical Package for the Social Sciences, 2 nd ed., pp. 276-372, Mc. Graw-Hill, New York, NY.,1975.

30. Fedors, R.F. "A Method for Estimating Both the Solubility Parameters and Molar Volumes of Liquids" Polym Eng. & Sci. 14(2), (1974) : 147-154.

31. Clarke, E.G.C. in Isolation and Identification of Drugs, Vol. 2, pp. 208, 486, 547, 548, The Pharmaceutical Press, London, 1975.

32. United States Pharmacopeial Convention, Inc., USP. XXI The United States Pharmacopeia - The National Formulary NF XVI, pp. 817-818, 989-990, Mack Publishing Company, Easton, PA.,1985.

33. Daniel, W.W. in Biostatistics : A Foundation For Analysis In The Health Sciences, 2 nd ed., pp. 254-296, John Wiley & Sons, New York, NY.,1978.

34. Guillory, J.K. "Heats of Transition of Methyl Prednisolone and Sulfathiazole by a Differential Thermal Analysis Method" J. Pharm. Sci. 56(1), (1967) : 72-75.

35. Windhol, M. in Merck Index, 10 th ed., pp. 62, 212, 721, 939, 940, 1275, 1513-1515, 2111, 3304, 3706, 3744, 3751, 4347, 4978, 5057, 5816, 5915, 6985, 7742, 7756, 9853, Merck & Co., Inc., Rahway, NJ., 1983.

36. Yost, R.W., Ettre, L.S. and Conlon, R.D. in Practical Liquid Chromatography: An Introduction, pp. 217-220, Perkin-Elmer Corp., Norwalk, CT.,1980.

37. Snyder, L.R. "solutions to Solution Problem-2" Chemtech. March (1980) : 188-193.

38. Weast, R.C. in Handbook of Chemistry and Physics, 54th ed., p. B 243, CRC Press, Cleveland, OH.,1973-1974.

39. Gennaro, A.R. in Remington's Pharmaceutical Sciences, 17 th ed., pp. 1067-1068, 1118, 1173, Mack Publishing Company, Easton, Pennsylvania, PA.,1985.

40. Reynolds, J.E.F. in Martindale : The Extra Pharmacopeia, 28 th ed., pp. 811, 1473-1475, The Pharmaceutical Press, London, 1982.

41. Bennett, D.R. in AMA Drug Evaluation, 5 th ed., pp. 1728, 1816, John Wiley & Sons, Inc., New York, NY.,1983.

42. Gilman, A.G., Goodman, L.S., and Gilman, A. in Goodman and Gilman's The Pharmacological Basis of Therapeutics, 6 th ed., pp. 350, 457, 1111, Macmillan Publishing Co., Inc., New York, NY.,1980.

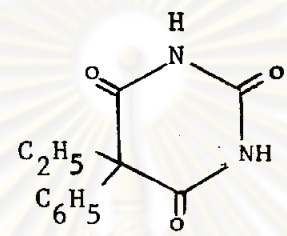
APPENDIX

Phenobarbital (35, 38-42)

Synonyms : Fenobarbital; Phenemalum; Phenobarbitone; Phenylethylmalonylurea.

Proprietary Names : Agrypnal; Barbenyl, Eskabarb; Fenemal; Gardenal; Luminal; Phenomet; T(h) eoloxin.

Chemical formula :



$C_{12}H_{12}N_2O_3$ = 232.24

5-Ethyl-5-phenyl-2,4,6 (1H, 3H, -5H) - pyrimidinetrione

5-Ethyl-5-phynylbarbituric acid

Description : White, odorless, glistening, small crystals, or a white crystalline powder, which may exhibit polymorphism; (slightly bitter taste;) stable in air; pH (saturated solution) about 5; pKa = 7.6, Mp. 174-178°C

Solubility : Soluble 1 g in about 1000 ml water, 8 ml alcohol, 13 ml ether, 40 ml chloroform, 700 ml benzene. Soluble in alkali hydroxides and carbonates.

Uses : Phenobarbital is classified into a long-acting barbiturate. This classical barbiturate is a sedative, hypnotic, and antiepileptic drug. In appropriate doses, it is used in neurosis and related tension states when mild, prolonged sedation is indicated, as in hypertension, coronary

artery disease, functional gastrointestinal disorders, and preoperative apprehension. In addition, it has specific usefulness in the symptomatic therapy of epilepsy. It is especially useful in patients with generalized tonic-clonic seizures (grand mal) and complex partial (psychomotor) seizures. Effective doses usually produce a degree of drowsiness or sluggishness.

Dose : Adult, usual : Oral, sedative, 30-120 mg in 2 or 3 divided doses; hypnotic, 100-320 mg; anticonvulsant, 50-100 mg 2 or 3 times a day. Usual range of dose, 30-600 mg daily.

Pediatric, usual : Oral, sedative, 2 mg/kg or 60 mg/m^2 body surface 3 times a day; hypnotic, individualized by physician; anticonvulsant or antidyskinetic, 3-5 mg/kg or 125 mg/m^2 body surface daily until a blood level of 10-15 µg/ml is attained.

Dosage Forms : Capsules : 15 mg

Capsules, extended release : 60 mg

Oral solution : 7.5 and 100 mg/5 ml

Tablets : 8, 15, 30, 60, and 100 mg

Elixir : 7.5 or 20 mg/5 ml

Toxicity : The adverse effects of phenobarbital have been reviewed by Brawning and Maynert (Symposium, 1972 a). Sedation, the most frequent undesired effect of phenobarbital, is apparent to some

extent in all patients upon initiation of therapy, but tolerance develops during chronic medication. Nystagmus and ataxia occur at excessive dosage. Phenobarbital sometimes produces irritability and hyperactivity in children and confusion in the elderly.

Scarlatiniformor morbilliform rash, possibly with other manifestations of drug allergy, occurs in 1 to 2 % of patients. Fatal exfoliative dermatitis is rare. Hypoprothrombinemia with hemorrhage has been observed in the newborn of mothers who have received phenobarbital during pregnancy; vitamin K is effective for treatment or prophylaxis. Megaloblastic anemia that responds to folate and osteomalacia that responds to high doses of vitamin D occur during chronic phenobarbital therapy of epilepsy, as they do during phenytoin medication.

Phenobarbital is readily absorbed, about 80 % of an oral dose and peak plasma levels are reached in 16-18 hours. Apparent volume of distribution is 0.7 - 1.0 L./kg. Therapeutic plasma levels range from 10 - 30 µg/ml. About 45 - 50 % of drug is bound to plasma protein. Apparent plasma half life varies from 50 - 120 hours in adults and 40 - 70 hours in children. Approximately 65 % of drug is metabolized and 35 % is excreted by the kidney unchanged. The main metabolite in man is the p-hydroxy-derivative, 5-ethyl-5-p-hydroxyphenyl barbituric acid. About 50 % is conjugated, less than 10 %, however, as the glucuronide. The rest is thought to be conjugated

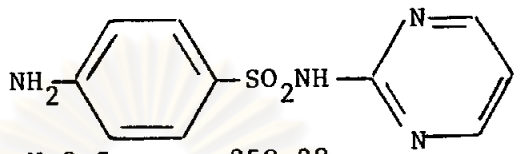
as the ethereal sulphate. Plasma clearance is slow and approximates 0.004 L/kg/hr.

Sulfadiazine (35, 38 - 42)

Synonyms : Sulphadiazine B.P ; Sulfadiazine U.S.P.

Proprietary Names : Adiazine, Microsulfon, Diazyl Dulcet, S-Diazine

Chemical formula :



$C_{10}H_{10}N_4O_2S$ = 250.28

4-Amino-N-2-pyrimidinylbenzene-sulfonamide

Description : White, yellowish-white, or pinkish-white, odorless or almost odorless, tasteless crystals or powder, slowly darkening on exposure to light.

Mp. 252-256°C with decomposition.

pK_a = 6.5 at 25°C

Solubility : Soluble 1 in 13,000 of water at 25°, 1 in 60 of boiling water, sparingly soluble in water at 37° : 13 mg/100 ml at pH 5.5 ; 200 mg/100 ml at pH 7.5 Soluble 1 in 300 of acetone; very slightly soluble in alcohol; practically insoluble in chloroform and ether; freely soluble in dilute mineral acids and in solutions of alkali hydroxides, carbonates and in ammonia water.

Uses : Sulfadiazine is the sulfonamide of choice for nocardiosis. Sulfadiazine may be administered for prophylaxis of rheumatic fever when other anti-infective agents (eg, penicillin G, erythromycin) cannot be used.

Sulfadiazine may be a preferred sulfonamide in certain other susceptible systemic infections (eg, in combination with pyrimethamine for toxoplasmosis or for prophylaxis of malaria where chloroquine resistant strains of Plasmodium falciparum are common).

Doses : The blood level should be maintained at 100-150 µg/ml

Oral : Adults, 2-4 g initially, then 1 g every 4-6 hours. Children and infants over 2 months, 75 mg/kg initially,

Then 150 mg/kg daily in 4-6 divided doses. The total daily dose should not exceed 6 g.

For prophylaxis of rheumatic fever, 500 mg once daily for patients under 30 kg and 1 g daily for those over 30 kg.

Intravenous : Adults, initially, 100 mg/kg up to a total of 5 g, then 30-50 mg/kg every 6-8 hours.

Children over 2 months, 50 mg/kg initially, then 100 mg/kg daily in 4 divided doses.

Oral therapy should be substituted as soon as possible

Dosage Forms : Sulfadiazine Tablets : 250, 300, 500 mg

Sulfadiazine Powder : 1 oz, 4 oz, 1 lb

Sulfadiazine Sodium Injection : 2.5 g/10 ml

Orally administered sulfadiazine is readily absorbed from the gastro-intestinal tract, peak blood concentration being reached 3-6 hours after a single dose. 20-55% of circulatoring sulfadiazine has been reported to be bound to plasma albumin. The drug is widely distributed in body fluids and tissues, and therapeutic concentrations are attained in the cerebrospinal fluid, usually more than half of those in the blood, within 4 hours of administration by mouth of a dose of 60 mg/kg body-weight.

Sulfadiazine is excreted somewhat slowly, about 50 % of a single dose by mouth being eliminated in 24 hours; between 15 % and 40 % of a dose is acetylated in the liver; both acetylated and unchanged drug are excreted by the kidney. The elimination half-life is 17 hours.

Crystalluria and related renal damage can be minimized by administration of adjuvant alkalinizing salts and by maintenance of an adequate 24-hr urine volume. To minimize crystalluria, sulfadiazine is also commonly combined with other sulfonamides.

Simple Linear Regression (33)

This is the most popular and frequently regression analysis method used in studying something about the relationship between two variables.

Simple Linear Regression Models

In the simple linear regression model two variables, X and Y, are of interest. The variable X is usually referred to as the independent variable, since it is under the control of the investigator, that is, values of X are selected by the investigator and, corresponding to each preselected value of X, one or more values of Y are obtained. The other variable, Y, accordingly, is called the dependent variable : Hence, it is the regression of Y on X.

The model is written as :

$$y = \alpha + \beta x + e \qquad \text{(Eq.27)}$$

where y is a typical value from one of the subpopulations of y, α and β are called population regression coefficients. Geometrically, α and β represent the y-intercept and slope, respectively, of the line on which all the means are assumed to lie. And e is called the error term

The method usually employed for obtaining the desired line is known as the method of least squares, and the resulting line is called the least-squares line. Hence, the general equation for a straight line is given by

$$y = a + bx \qquad \text{(Eq.28)}$$

where y is a value on the vertical axis, x is a value on the horizontal axis, a is the point where the line crosses the vertical axis, the y-intercept, and b shows the amount by which the line rise for each unit increase in x, the slope of the line. a and b can be obtained from the following equations :

$$a = \frac{\sum_{i=1}^{n} Y_i - b \sum_{i=1}^{n} X_i}{n} \qquad \text{(Eq.29)}$$

$$b = \frac{n \sum_{i=1}^{n} X_i Y_i - \left(\sum_{i=1}^{n} X_i\right)\left(\sum_{i=1}^{n} Y_i\right)}{n \sum_{i=1}^{n} X_i^2 - \left(\sum_{i=1}^{n} X_i\right)^2} \qquad \text{(Eq.30)}$$

Analysis of Variance Results

ANOVA Table for Simple Linear Regression

Source of variation	SS	df	MS
Regression	$SSR = b \sum_{i=1}^{n} X_i Y_i$	1	MSR = SSR/1
Error	$SSE = \sum_{i=1}^{n} Y_i^2 - b \sum_{i=1}^{n} X_i Y_i$	n-2	MSE = SSE/(n-2)
Total	$SSTO = \sum_{i=1}^{n} Y_i^2$	n-1	

Coefficient of Determination (R^2)

It is intuitively appealing to speculate that if a regression equation does a good job of describing the relationship between two variables, the explained sum of squares should constitute a large proportion of the total sum of squares. This is exactly what is done in evaluating a regression equation based on sample data, and the result is called the sample coefficient of determination, R^2, calculating using an equation :

$$R^2 = \frac{SSR}{SSTO} \qquad \text{(Eq.31)}$$

$$= \frac{b^2\left[\sum_{i=1}^{n} X_i^2 - \left(\sum_{i=1}^{n} X_i\right)^2/n\right]}{\sum_{i=1}^{n} Y_i^2 - \left(\sum_{i=1}^{n} Y_i\right)^2/n} \qquad \text{(Eq.32)}$$

Polynomial Regression (28, 29)

This is the most frequently used curvilinear response model in practice, because of its ease in handling as a special case of the general linear regression model.

Polynomial Regression Models

Polynomial regression models can contain one, two, or more than two independent variables. Furthur, the independent variable can be present in various powers.

One Independent Variable-Second Degree has been used in this investigation because the true response function is unknown, but a second degree polynomial is a good approximation to the true function.

The model is written as :

$$y_i = \beta_0 + \beta_1 X_i + \beta_2 X_i^2 + \varepsilon_i \qquad \text{(Eq.33)}$$

As can be seen, the independent variable appears in the second degree. Assuming that $E(\varepsilon_i) = 0$, the response function for model (Eq. 33) is

$$E(y) = \beta_0 + \beta_1 x + \beta_2 x^2 \qquad \text{(Eq.34)}$$

which is a parabola and is frequently called a quadratic response function.

The regression coefficient β_0 represents the mean response of y when x = 0 if the scope of the model includes x = 0, otherwise, β_0 has no separate meaning of its own in the model. The regression coefficient β_1 is often called the linear effect coefficient while β_2 is called the curvature effect coefficient.

Fitting of Model

The least squares normal equations for the second-order polynomial are

$$x'xb = x'y$$

where ;

$$b = \begin{bmatrix} b_0 \\ b_1 \\ b_2 \end{bmatrix}, \quad x'x = \begin{bmatrix} n & \Sigma x_i & \Sigma x_i^2 \\ \Sigma x_i & \Sigma x_i^2 & \Sigma x_i^3 \\ \Sigma x_i^2 & \Sigma x_i^3 & \Sigma x_i^4 \end{bmatrix}, \quad x'y = \begin{bmatrix} \Sigma y_i \\ \Sigma x_i y_i \\ \Sigma x_i^2 y_i \end{bmatrix}$$

This yields the normal equations in terms of the algebraic version as :

$$\begin{aligned} \Sigma y_i &= nb_0 + b_1\Sigma x_i + b_2\Sigma x_i^2 \\ \Sigma x_i y_i &= b_0\Sigma x_i + b_1\Sigma x_i^2 + b_2\Sigma x_i^3 \\ \Sigma x_i^2 y_i &= b_0\Sigma x_i^2 + b_1\Sigma x_i^3 + b_2\Sigma x_i^4 \end{aligned} \qquad \text{(Eq. 35)}$$

Analysis of Variance Results

ANOVA Table for Second-Order Polynomial Model

Source of variation	SS	df	MS
Regression	$SSR = b'x'y - n\bar{y}^2$	2	$MSR = SSR/2$
Error	$SSE = y'y - b'x'y'$	n-3	$MSE = SSE/n-3$
Total	$SSTO = y'y - n\bar{y}^2$	n-1	

where ; $b' = \begin{bmatrix} b_0 & b_1 & b_2 \end{bmatrix}$, $\bar{y} = \Sigma y_i/n$, $y'y = \Sigma y_i^2$

Coefficient of Multiple Determination (R^2)

For a descriptive measure of the degree of relation between x_i and y_i, the R^2 is used and calculated using an equation

$$R^2 = \frac{SSR}{SSTO} \qquad \text{(Eq. 36)}$$

Multiple Regression (28, 29)

Multiple regression analysis is one of the most widely used of all statistical tools because of the matrix expressions for multiple regression are the same as for simple regressions, and it is also highly useful in experimental situations where the experimenter can control the independent variables.

Multiple Regression Models

Multiple regression models can contain one dependent variable (y_i) and one, two, or more than two independent variables (x_i)

Three independent variables have been used in this investigation because the true response function is unknown and depends on these independent variable values. Hence, a multiple regression is a good approximation to the true function

The model is written as :

$$y_i = \beta_0 + \beta_1 x_{1i} + \beta_2 x_{2i} + \beta_3 x_{3i} + \varepsilon_i \qquad \text{(Eq. 37)}$$

It is called a first-order model with three independent variables. y_i denotes as usual the response in the i th trial, and x_{1i}, x_{2i}, x_{3i} are the values of the three independent variables in the i th traial. The parameters of the model are β_0, β_1, β_2, and β_3, and the error term is ε_i.

Assuming that E (ε_i) = 0, the regression function for model (Eq. 37) is :

$$E(y) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 \qquad \text{(Eq. 38)}$$

The regression coefficient β_0 represents the mean response of y when $x_1 = x_2 = x_3 = 0$ if the scope of the model includes $x_1 = x_2 = x_3 = 0$ otherwise, β_0 has no separate meaning of its own in the model. β_1, β_2, β_3 are called the linear regression coefficient.

Fitting of Model

The least squares normal equations for the first-order multiple regression are

$$x'xb = x'y$$

where ;

$$b = \begin{bmatrix} b_0 \\ b_1 \\ b_2 \\ b_3 \end{bmatrix}$$

$$x'x = \begin{bmatrix} n & \Sigma x_{1i} & \Sigma x_{2i} & \Sigma x_{3i} \\ \Sigma x_{1i} & \Sigma x_{1i}^2 & \Sigma x_{1i}x_{2i} & \Sigma x_{1i}x_{3i} \\ \Sigma x_{2i} & \Sigma x_{1i}x_{2i} & \Sigma x_{2i}^2 & \Sigma x_{2i}x_{3i} \\ \Sigma x_{3i} & \Sigma x_{1i}x_{3i} & \Sigma x_{2i}x_{3i} & \Sigma x_{3i}^2 \end{bmatrix}$$

$$x'y = \begin{bmatrix} \Sigma y_i \\ \Sigma x_{1i}y_i \\ \Sigma x_{2i}y_i \\ \Sigma x_{3i}y_i \end{bmatrix}$$

This yields the normal equations in terms of the algebraic version as :

$$\Sigma y_i = nb_0 + b_1\Sigma x_{1i} + b_2\Sigma x_{2i} + b_3\Sigma x_{3i}$$

$$\Sigma x_{1i}y_i = b_0\Sigma x_{1i} + b_1\Sigma x_{1i}^2 + b_2\Sigma x_{1i}x_{2i} + b_3\Sigma x_{1i}x_{3i}$$

(Eq. 39)

$$\Sigma x_{2i}y_i = b_0\Sigma x_{2i} + b_1\Sigma x_{1i}x_{2i} + b_2\Sigma x_{2i}^2 + b_3\Sigma x_{2i}x_{3i}$$

$$\Sigma x_{3i}y_i = b_0\Sigma x_{3i} + b_1\Sigma x_{1i}x_{3i} + b_2\Sigma x_{2i}x_{3i} + b_3\Sigma x_{3i}^2$$

Analysis of Variance Results

ANOVA Table for Multiple Regression Model.

Source of variation	SS	df	MS
Regression	$SSR = b'x'y - n\bar{y}^2$	3	$MSR = SSR/3$
Error	$SSE = y'y - b'x'y$	n-4	$MSE = SSE/_{(n-4)}$
Total	$SSTO = y'y - n\bar{y}^2$	n-1	

where ; $b' = \left[b_0 \quad b_1 \quad b_2 \quad b_3 \right]$, $\bar{y} = y_i/n$

$y'y = y_i^2$

Coefficient of Multiple Determination (R^2)

For a descriptive measure of the degree of relation between x_{1i}, x_{2i}, x_{3i} and y_i, the R^2 is used and calculated using an equation

$$R^2 = \frac{SSR}{SSTO} \qquad \text{(Eq. 40)}$$

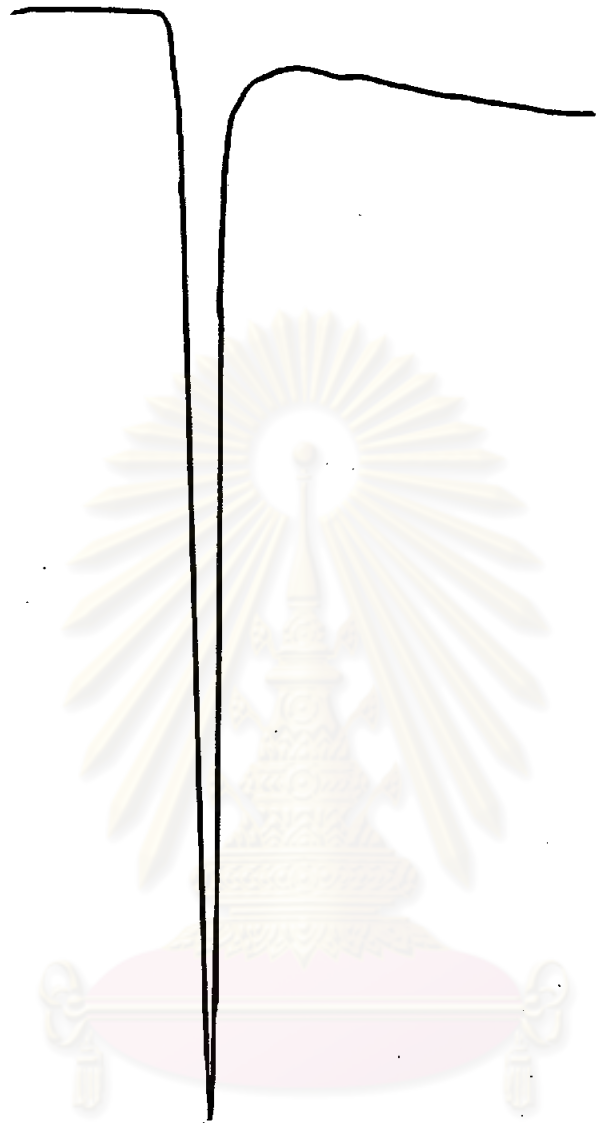


Fig 3 : Thermogram of phenobarbital obtained using DSC, sensitivity 1.00 m cal/sec

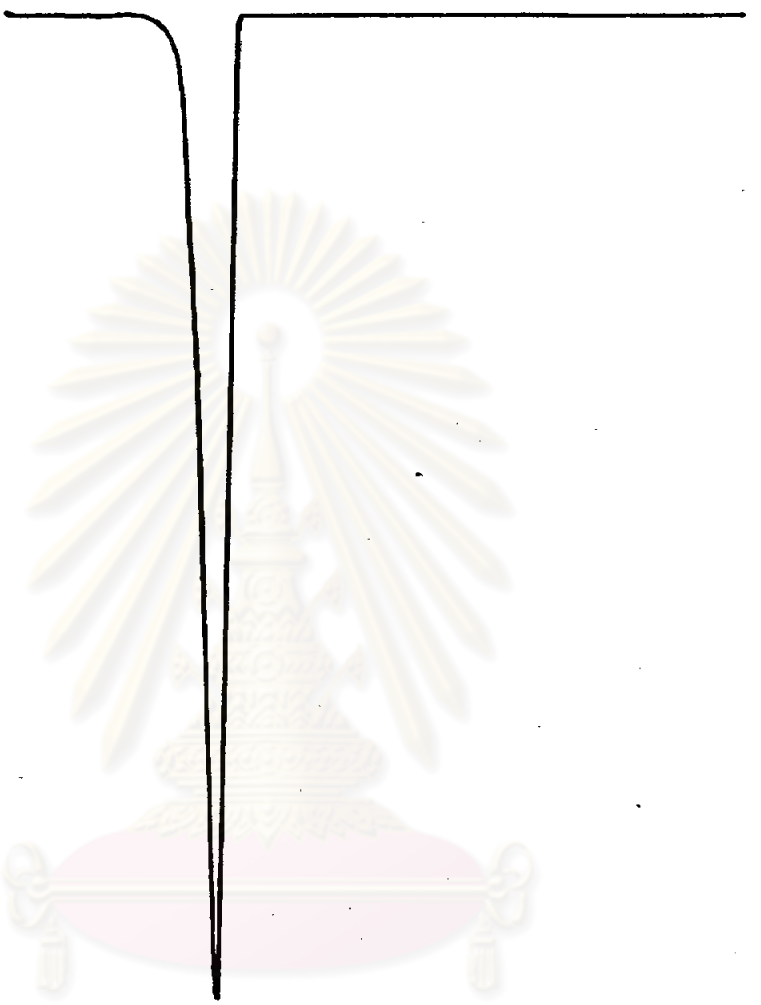


Fig 4 : Thermogram of indium obtained using DSC, sensitivity 1.00 m cal/sec

VITA

Name Mrs. Sukanya Khongthanarat

Education Bachelor of Science in Pharmacy in 1975, Faculty of Pharmaceutical Sciences, Chulalongkorn University Bangkok, Thailand