VERWYSINGS

AGINS BD, BERMAN DS, SPICEHANDLER D, EL-SADR W, SIMBERKOFF MS, RAHAL JJ. Effect of combined therapy with ansamycin, clofazimine, ethambutol, and isoniazid for *Mycobacterium avium* infection in patients with AIDS. *Journal of Infectious Diseases* 159: 784-787. **1989**.

AMBUDKAR SV, LELONG IH, ZHANG J, CARDARELLI CO, GOTTESMAN MM, PASTAN I. Partial purification and reconstitution of the human multidrug-resistance pump: Characterization of the drug-stimulatable ATP hydrolysis. *Proceedings of the National Academy of Sciences of the United States of America* 89: 8472 - 8476. **1992**.

AMES GF. Bacterial periplasmic transport systems: Structure, mechanism and evolution. *Annual Review of Biochemistry* 55: 397-425. **1986**.

ANDERSON R, ZEIS BM, ANDERSON IF. Clofazimine-mediated enhancement of reactive oxidant production by human phagocytes as a possible therapeutic mechanism. *Dermatologica* 176: 234-242. **1988**.

ANDERSON R, SMIT MJ. Clofazimine and B669 inhibit the proliferative responses and Na^+,K^+ adenosine triphosphatase activity of human lymphocytes by a lysophospholipid-dependent mechanism. *Biochemical Pharmacology* 46: 2029-2038. **1993**.

ANDERSON R. THERON AJ. FELDMAN C. Membrane-stabilizing, anti-inflammatory interactions of macrolides with human neutrophils. *Inflammation* 20(6):693-705. **1996.**

ARCECI RJ, CROOP JM, HORWITZ SB, HOUSMAN D. The gene encoding multidrug resistance is induced and expressed at high levels during pregnancy in the secretory epithelium of the uterus. *Proceedings of the National Academy of Sciences of the United States of America* 85: 4350-4354. **1988**.

ARSENAULT AL, LING V, KARTNER N. Altered plasma membrane ultrastructure in multidrug-resistant cells. *Biochimica et Biophysica Acta* 938: 315-321. **1988**.

BARRY VC, BELTON JG, CONALTY ML, DENNENY JM, EDWARD DW, O'SULLIVAN JF, TWOMEY D, WINDER F. A new series of phenazines (rimino-compounds) with high antituberculosis activity. *Nature (London)* 179: 1013-1015. **1957**.

BARRY VC, CONALTY ML. The antimycobacterial activity of B663. *Leprosy Review* 36: 3-7. **1965**.

BECKER WM, DEAMER DW. The chemistry of the cell: The importance of selelectively permeable membranes. *In*: The world of the cell. Second edition. The Benjamin/Cummings Publishing Company, Inc. Pp 24 - 31. **1991a**.

BECKER WM, DEAMER DW. Cells an organelles: The plasma membrane. *In*: The world of the cell. Second edition. The Benjamin/Cummings Publishing Company, Inc. Pp 83 - 85. **1991b**.

BECKER WM, DEAMER DW. Membranes: Their structure and chemistry. *In*: The world of the cell. Second edition. The Benjamin/Cummings Publishing Company, Inc. Pp 158 - 192. **1991c**.

BECKER WM, DEAMER DW. Transport across membranes: Overcoming the permeability barrier. *In*: The world of the cell. Second edition. The Benjamin/Cummings Publishing Company, Inc. Pp 193-219. **1991d**.

BERGELSON LD, DYATLOVITSKAYA EV, TORKHOVSKAYA TI, SOROKINA IB, GORKOVA NP. Phospholipid composition of membranes in the tumor cell. *Biochimica et Biophysica Acta* 210: 287 - 298. **1970**.

BERGER SH, JEHN CH, JOHNSON LF, BERGER FG. Thymidylate synthase overproduction and gene amplification in fluorodeoxyuridine-resistant human cells. *Molecular Pharmacology* 28: 461 - 467 . **1985**.

BIEDLER JL, RIEHM H, PETERSON RHF, SPENGLER BA. Membrane-mediated drug resistance and phenotypic reversion to normal growth behavior of Chinese hamster cells. *Journal of the National Cancer Institute* 55: 671-680. **1975**.

BOLHUIS H, VAN VEEN HW, MOLENAAR D, POOLMAN B, DRIESSEN AJM, KONINGS WN. Multidrug resistance in *Lactococcus lactis*: Evidence for ATP-dependent drug extrusion from the inner leaflet of the cytoplasmic membrane. *EMBO Journal* 15: 4239 - 4249. **1996a**.

BOLHUIS H, VAN VEEN HW, BRANDS JR, PUTMAN M, POOLMAN B, DRIESSEN AJM, KONINGS WN. Energetics and mechanism of drug transport mediated by the lactococcal MDR transporter LmrP. *Journal of Biological Chemistry* 271: 24123 - 24128. **1996b**.

BOLHUIS H, VAN VEEN HW, POOLMAN B, DRIESSEN AJ, KONINGS WN. Mechanisms of multidrug transporters. *FEMS Micorbiology Reviews* 21: 55-84. **1997**.

BORST P. DNA amplification and multidrug resistance. *Nature* 309: 580. **1984**.

BOSCOBOINIK D, DEBANNE MT, STAFFORD AR, JUNG CY, GUPTA RS, EPLAND RM. Dimerization of the P-glycoprotein in membranes. *Biochimica et Biophysica Acta* 1027: 225 - 228. **1990**.

BRADLEY G, GEORGES E, LING V. Sex-dependent and independent expression of the P-glycoprotein isoforms in Chinese hamster. *Journal of Cellular Physiology* 145: 398-408. **1990**.

BUCANA CD, GIAVAZZI R, NAYAR R, O'BRIAN CA, SEID C, EARNEST LE, FAN D. Retention of vital dyes correlates inversely with the multidrug-resistant phenotype of adriamycin-selected murine fibrosarcoma variants. *Experimental Cell Research* 190: 69-75. **1990**.

CHAN HS, THORNER PS, HADDAD G, LING V. Immunohistochemical detection of P-glycoprotein: Prognostic correlation in soft tissue sarcoma of childhood. *Journal of Clinical Oncology* 8: 689-704. **1990**.

CHAN HS, DE BOER G, HADDAD G, GALLIE BL, LING V. Multidrug resistance in pediatric malignancies. *Hematology/Oncology Clinics of North America* 9: 275-318. **1995**.

CHAUDHARY PM, RONINSON IB. Expression and activity of P-glycoprotein, a multidrug efflux pump, in human hematopoietic stem cells. *Cell* 66: 85-94. **1991**.

CHAUDHARY PM, MECHETNER EB, RONINSON IB. Expression and activity of the multidrug resistance P-glycoprotein in human peripheral blood lymphocytes. *Blood* 80: 2735-2739. **1992**.

CHEN CJ, CHIN JE, UEDA K, CLARK DP, PASTAN I, GOTTESMAN MM, RONINSON IB. Internal duplication and homology with bacterial transport proteins in the mdr1 (P-glycoprotein) gene from multidrug-resistant human cells. *Cell* 47: 381 - 389. **1986**.

CHEN CJ, CLARK D, UEDA K, PASTAN I, GOTTESMAN MM, RONINSON IB. Genomic oraganization of the human multidrug resistance (MDR1) gene and origin of P-glycoproteins. *Journal of Biological Chemistry* 265: 506 - 514. **1990**.

CHEN X, BASTOW K, GOZ B, KUCERA LS, MORRIS-NATSCHKE SL, ISHAQ KS. Synthesis and evaluation of novel thymidine analogs as antitumor and antiviral agents. *Journal of Medicinal Chemistry* 39: 3412-3417. **1996**.

CHIN JE, SOFFIR R, NOONAN KE, CHOI K, RONINSON IB. Structure and expression of the human MDR (P-glycoprotein) gene family. *Molecular & Cellular Biology* 9: 3808-3820. **1989**.

CHIN K-V, CHAUHAN SS, ABRAHAM I, SAMPSON KE, KROLCZYK AJ, WONG M, SCHIMMER P, PASTAN I, GOTTESMAN MM. Reduced mRNA levels for the multidrug-resistance genes in cAMP-dependent protein kinase mutant cell lines. *Journal of Cellular Physiology* 152: 87-94. **1992**.

CHONG ASF, MARKHAM PN, GEBEL HM, BINES SD, COON JS. Diverse-multidrug-resistance-modification agents inhibit cytolytic activity of natural killer cells. *Cancer Immunology, Immunotherapy* 36: 133-139. **1993**.

CLARKE AR, PURDIE CA, HARRISON DJ, MORRIS RG, BIRD CC, HOOPER ML, WYLLIE AH. Thymocyte apoptosis induced by p53-dependent and independent pathways. *Nature* 362: 849 - 852. **1993**.

COLEY HM, TWENTYMAN PR, WORKMAN P. Improved cellular accumulation is characteristic of anthracyclines which retain high activity in multidrug resistant cell lines, alone or in combination with verapamil or cyclosporin A. *Biochemical Pharmacology* 38: 4467-4475. **1989**.

CROOP JM. P-glycoprotein stucture and evolutionary homologies. *In*: Mulitple drug resistance in cancer: Cellular, molecular and clinical approaches. (Reprinted from Cytotechnology, volume 12, 1993). Clynes M, ed. Kluwer Academic Publishers. Pp 1-32. **1994**.

DANO K. Active outward transport of daunomycin in resistant Ehrlich ascites tumor cells. *Biochimica et Biophysica Acta* 323: 466 - 483. **1973**.

DEN BOER ML, PIETERS R, KAZEMIER KM, ROTTIER MM, ZWAAN CM, KASPERS GJ, JANKA-SCHAUB G, HENZE G, CREUTZIG U, SCHEPER RJ, VEERMAN AJ. Relationship between major vault protein/lung resistance protein, multidrug resistance-associated protein, P-glycoprotein expression, and drug resistance in childhood leukemia. *Blood* 91: 2092-2098. **1998**.

DESIKAN KV, BALAKRISHNAN S. Tissue levels of clofazimine in case of leprosy. *Leprosy Review* 47: 107 - 113. **1976**.

DOIGE CA, YU X, SHAROM FJ. The effects of lipids and detergents on ATPase-active P-glycoprotein. *Biochimica et Biophysica Acta* 1146: 65-72. **1993**.

DRACH D, ZHAO S, DRACH J, MAHADEVIA R, GATTRINGER C, HUBER H, ANDREEFF. Subpopulations of normal peripheral blood and bone marrow cells express a functional multidrug resistant phenotype. *Blood* 80: 2729-2734. **1992**.

DURANDT C, VAN RENSBURG CEJ, THERON AJ, CHASEN M. Novel riminophenazine compounds with improved anti-tumour properties. *South-African Journal of Sciences* 92: 257-259. **1996**.

DURANDT C. Immuunregulerende, anti-mikrobiese en anti-tumor aktiwiteit van nuwe riminofenasiene. Voorgelê te vervulling van die vereistes vir die graad M.Sc (Geneeskundige Immunologie), Universiteit van Pretoria. **1994**.

ENDICOTT JA, LING V. The biochemistry of P-glycoprotein-mediated multidrug resistance. *Annual Review of Biochemistry* 58: 137-171. **1989**.

EWIG RAG, KOHN KW. DNA damage and repair in mouse leukemia L1210 cells treated with nitrogen mustard, 1,3-bis(2-chloroethyl)-1-nitrosourea, and other nitroureas. *Cancer Research* 37: 2114 - 2122. **1977**.

EYTAN GD, REGEV R, ASSARAF YG. Functional reconstitution of P-glycoprotein reveals an apparent near stoichiometric drug transport to ATP hydrolysis. *Journal of Biological Chemistry* 271: 3172 - 3178. **1996**.

FAN D, BELTRAN PJ, O'BRIAN CA. Reversal of multidrug resistance. *In*: Reversal of multidrug resistance in cancer. Kellen JA, ed. CRC Press. Pp 93-125. **1994**.

FERTE J. Analysis of the tangled relationships between P-glycoprotein-mediated multidrug resistance and the lipid phase of the cell membrane. *European Journal of Biochemistry* 267(2): 277-294. **2000**

FINK D, NEBEL S, NORRIS PS, KIM HK, HAAS M, HOWELL SB. The effect of different chemotherapeutic agents on the enrichment of DNA mismatch repair-deficient tumour cells. *British Journal of Cancer* 77: 703-708. **1998**.

FOJO AT, WHANG-PENG J, GOTTESMAN MM, PASTAN I. Amplification of DNA sequences in human multidrug-resistant KB carcinoma cells. *Proceedings of the National Academy of Sciences of the of the United States of America* 82: 7661-7665. **1985**.

FOJO AT, UEDA K, SLAMON DJ, POPLACK DG, GOTTESMAN MM, PASTAN I. Expression of multidrug resistance gene in human tumors and tissues. *Proceedings of the National Academy of Sciences of the of the United States of America* 84: 265-269. **1987**.

FORD JM, HAIT WN. Pharmacologic circumvention of multidrug resistance. *In*: Multiple drug resistance in cancer: Cellular, molecular and clinical approaches. (Reprinted from Cytotechnology, volume 12, 1993). Clynes M, ed. Kluwer Academic Publishers. Pp 171-212. **1994**.

FORD JM. Modulators of multidrug resistance: Preclinical studies. *Hematology/ Oncology Clinics of North America* 9: 337-361. **1995**.

FORD JM. Experimental reversal of P-glycoprotein-mediated multidrug resistance by pharmacological chemosensitisers. *European Journal of Cancer* 32A: 991 - 1001. **1996**.

FORD JM, YANG J-M, HAIT WN. P-glycoprotein-mediated multidrug resistance: Experimental and clinical strategies for its reversal. *In*: Drug resistance. Hait WN, ed. Cancer Treatment and Research. Freireich EJ, Series Editor. Kluwer Academic Publishers. Pp 3-38. **1996**.

FRANZBLAU SG, WHITE KE, O'SULLIVAN JF. Structural-activity relationships of tetramethylpiperidine-substituted phenazines against *Mycobacterium leprae in vitro*. *Antimicrobial Agents & Chemotherapy* 33: 2004 - 2005. **1989**.

FREUND JE, SIMON GA. The coefficient of correlation. *In:*Statistics: A first course. Sixth edition. Prentice Hall, Inc. Pp. 461 – 467. **1995**.

FRICHE E, DEMANT EJ, SEHESTED M, NISSEN NI. Effect of anthracycline analogs on photolabelling of P-glycoprotein by [^{125}I]iodomycin and [^{3}H]azidopine: Relation to lipophilicity and inhibition of daunorubicin transport in multidrug resistant cells. *British Journal of Cancer* 67: 226-231. **1993**.

GANONG WF. Circulating Body Fluids: Red Blood Cells. *In*: Review of Medical Physiology. Fifteenth Edition. Appleton & Lange. Pp 490 – 492. **1991**.

GARRELTS JC. Clofazimine: A review of its use in leprosy and *Mycobacterium avium* complex infection. *DICP* 25: 525-531. **1991**.

GARRIGOS M, MIR LM, ORLOWSKI S. Competitive and non-competitive inhibition of the multidrug-resistance-associated P-glycoprotein ATPase: Further Experimental evidence for a multisite model. *European Journal of Biochemistry* 244: 664-673. **1997**.

GERLACH JH, KARTNER N, BELL DR, LING V. Multidrug resistance. *Cancer Surveys* 5: 25-46. **1986a**.

GERLACH JH, ENDICOTT JA, JURANKA PF, HENDERSON G, SARANGI F, DEUCHARS KL, LING V. Homology between P-glycoprotein and a bacterial haemolysin transport protein suggests a model for multidrug resistance. *Nature* 324: 485-489. **1986b**.

GERLACH JH. Structure and function of P-glycoprotein. *In*: Drug resistance in cancer therapy. Ozols RF, ed. Kluwer Academic Publishers. Pp 37-53. **1989**.

GERMANN UA. Molecular analysis of the multidrug transporter. *In*: Multiple drug resistance in cancer: Cellular, molecular and clinical approaches (Reprinted from Cytotechnology, volume 12, 1993). Clynes M, ed. Kluwer Academic Publishers. Pp 33 - 62. **1994**.

GILL DR, HYDE S. HIGGINS CF, VALVERDE MA, MINTENIG GM, SEPULVEDA FV. Seperation of drug transport and chloride channel functions of the human multidrug resistance P-glycoprotein. *Cell* 71: 23 - 32. **1992**.

GOASGUEN JE, DOSSOT J-M, FARDEL O, LE MEE F, LE GALL E, LEBLAY R, LEPRISE PY, CHAPERON J, FAUCHET R. Expression of the multidrug resistance-associated P-glycoprotein (P-170) in 59 cases of *de novo* acute lymphoblastic leukemia:Prognositc Implications. *Blood* 81: 2394 - 2398. **1993**.

GOLDSTEIN LJ, GALSKI H, FOJO A, WILLINGHAM M, LAI S-L, GAZDAR A, PIRKER R, GREEN A, CRIST W, BRODEUR GM, LIEBER M, COSSMAN J, GOTTESMAN MM, PASTAN I. Expression of a multidrug resistance gene in human cancers. *Journal of the National Cancer Institute* 81: 116-124. **1989**.

GOLDSTEIN LJ. Clinical reversal of drug resistance. *Current Problems in Cancer* 19: 65 - 124. **1995**.

GOSLAND MP, VORE M, GOODIN S, TSUBOI C. Estradiol-17β-(β-D-glucoronide): a cholestatic organic anion and substrate for the multidrug resistance transporter. *Proceedings of the American Associtaion of Cancer Research* 34: 1842. **1993**.

GOTTESMAN MM, PASTAN I. The multidrug transporter, a double-edged sword. *Journal of Biological Chemistry* 263: 12163-12166. **1988**.

GOTTESMAN MM. How cancer cells evade chemotherapy: Sixteenth Richard and Hinda Rosenthal Foundation Award Lecture. *Cancer Research* 53: 747 - 754. **1993**.

GOTTESMAN MM, PASTAN I. Biochemistry of multidrug resistance mediated by the multidrug transporter. *Annual Review of Biochemistry* 62: 385 - 427. **1993**.

GOTTESMAN MM, PASTAN I, AMBUDKAR SV. P-glycoprotein and multidrug resistance. *Current Opinion in Genetics & Development* 6: 610-617. **1996**.

GREENBERGER LM, LOTHSTEIN L, WILLIAMS SS, HORWITZ SB. Distinct P-glycoprotein precursors are overproduced in independently isolated drug-resistant cell lines. *Proceedings of the National Academy of Sciences of the United States of America* 85: 3762 - 3766. **1988**.

GROS P, CROOP J, HOUSMAN D. Mammalian multidrug resistance gene: Complete cDNA sequence indicates homology to bacterial transport proteins. *Cell* 47: 371 - 380. **1986**.

GRUBER A, VITOLS S, NORGREN S, ARESTROM I, PETERSON C, BJORKHOLM M, REISENSTEIN P, LUTHMAN H. Quantitative determination of *mdr1* gene expression in leukaemic cells from patients with acute leukemia. *British Journal of Cancer* 66: 266-272. **1992**.

GUYTON AC, HALL JE. The cell and its function. *In*: Textbook of medical physiology. Ninth edition. WB Sanders Company. Pp 11-14. **1996a**.

GUYTON AC, HALL JE. Transport of ions and molecules through the cell membrane. *In*: Textbook of medical physiology. Ninth edition. WB Sanders Company. Pp 43-55. **1996b**.

HARRISON DJ. Molecular mechanims of drug resistance in tumours. *Journal of Pathology* 175: 7-12. **1995**.

HASMANN M, VALET GK, TAPIERO H, TREVORROW K, LAMPIDIS T. Membrane potential differences between adriamycin-selected and -resistant cells as measured by flow cytometry. *Biochemical Pharmacology* 38: 305-312. **1989**.

HIGGINS CF, GOTTESMAN MM. Is the multidrug transporter a flippase? *Trends in Biochemical Sciences* 17: 18-22. **1992**.

HILGARD P, STEKAR J, VOEGELI R, ENGEL J, SHUMACKER W, EIBL H, UNGER C, BERGER MR. Characterization of the anti-tumor activity of hexadecylphophocholine (D18506). *European Journal of Cancer & Clinical Oncology* 24: 1457 - 1461. **1988**.

HIPFNER DR, DEELEY RG, COLE SP. Structural, mechanistic and clinical aspects of MRP1. *Biochimica et Biophysica Acta* 1461(2): 359 – 376. **1999**.

HOLZMAYER TA, HILSENBECK S, VON HOFF DD, RONINSON IB. Clinical correlates of MDR1 (P-glycoprotein) gene expression in ovarian and small-cell lung carcinomas. *Journal of the National Cancer Institute* 84: 1486-1491. **1992**.

HOMOLYA L, HOLLO Z, GERMANN UA, PASTAN I, GOTTESMAN MM, SARKADI I. Fluorescent cellular indicators are extruded by the multidrug resistance protein. *Journal of Biological Chemistry* 268: 21493 - 21496. **1993** .

HUDGINS WR, SHACK S, MYERS CE, SAMID D. Cytostatic activity of phenylacetate and derivatives against tumor cells: Correlation with lipophilicity and inhibition of protein penylation. *Biochemical Pharmacology* 50: 1273-1279. **1995**.

IWADATE Y, TAGAWA M, FUJIMOTO S, HIROSE M, NAMBA H, SUEYOSHI K, SAKIYAMA S, YAMAURA A. Mutation of the p53 gene in human astrocytic tumours correlates with increased resistance to DNA-damaging agents but not to anti-microtubule anti-cancer agents. *British Journal of Cancer* 77: 547-551. **1998**.

JOHNSON AG. Correlation: How strong is the relationship? *In*: Statistics. Merton RK, ed. Harcourt Brace Jovanovich, Publishers. Pp. 171 – 180. **1988**.

JULIANO RL, LING V. A surface glycoprotein modulating drug permeability in Chinese hamster ovary cell mutants. *Biochimica et Biophysica Acta* 455: 152-162. **1976**.

KAGAN VE. Tocopherol stabilizes membranes against phopholipase A, free fatty acids and lysophospholipids. *Annals of the New York Academy of Sciences* 570: 121-135. **1989**.

KELLEN JA. Multidrug resistance: Introduction. *In*: Reversal of multidrug resistance in cancer. Kellen JA, ed. CRC Press. Pp 1-19. **1994**.

KESSEL D, BOTTERILL V, WODINSKY I. Uptake and retension of daunomycin by mouse leukemic cells as factors in drug response. *Cancer Research* 28: 938-941. **1968**.

KESSEL D, BECK WT, KUKURUGA D, SCHULTZ V. Characterization of multidrug resistance by fluorescent dyes. *Cancer Research* 51: 4665 - 4670. **1991**.

KRAJEWSKA MM, ANDERSON R. An *in vitro* comparison of the effects of the prooxidative riminophenazines clofazimine and B669 on neutrophil phopholipase A_2 activity and superoxide generation. *Journal of Infectious Diseases* 167: 899-904. **1993**.

LABROILLE G, BELLOC F, BILHOU-NABERA C, BONNEFILLE S, BASCANS E, BOISSEAU MR, BERNARD P, LECOMBE F. Cytometric study of intracellular P-gp expression and reversal of drug resistance. *Cytometry* 32:86 – 94. **1998**.

LATHAM PM. The pharmacokinetics basis of therapeutics. *In*: Pharmacology: An illustrated review with questions and explanations. Third edition. Ebadi M, ed. Little, Brown and Company. Pp 3-12. **1996**.

LIJNEN P, HUYSECOM J, FAGARD P, STAESSEN J, AMERY A. Inhibition of human erythrocyte and leucocyte Na^+, K^+-pump activity by lysophophatidylcholines. *Methods & Findings in Experimental & Clinical Pharmacology* 12: 281-286. **1990**.

LING V, THOMPSON LH. Reduced permeability in CHO cells as a mechanism of resistance to colchicine. *Journal of Cellular Physiology* 83: 103-116. **1974**.

LIU C, QURESHI IA, DING X-J, SHAN Y-F, HUANG Y-W, XIE Y, JI MR. Modulation of multidrug resistance gene (*mdr1*) with antisense oligodeoxynucleotides. *Clinical Science* 91: 93 - 98. **1996**.

LOO TW, CLARKE DM. Merck Frost Award Lecture 1998. Molecular dissection of the human multidrug resistance P-glycoprotein. *Biochemistry & Cell Biology* 77(1): 11 – 23. **1999**

LUDESCHER C, PALL G, IRSCHICK EU, GASTL G. Differential activity of P-glycoprotein in normal blood lymphocytes subsets. *British Journal of Haematology* 101:722 – 727. **1998**.

LUM BL, GOSLAND MP, KAUBISCH S, SIKIC BI. Molecular targets in oncology: Implications of the multidrug resistance gene. *Pharmacotherapy* 13: 88-109. **1993**.

MAFTAH A, HUET O, GALLET P-F, RATINAUD M-H. Flow cytometry's contribution to the measurement of cell functions. *Biology of the Cell* 78: 85 - 93. **1993**.

MALORNI W, LUCIA MB, RAINALDI G, CAUDA R, CIANFRIGLIA M, DONELLI, G, ORTONA, L. Intracellular expression of P-170 glycoprotein in peripheral blood mononuclear cell subsets from healthy donors and HIV-infected patients. *Haematologica* 83:13 – 20. **1998**.

MARIE J-P, ZITTOUN R, SIKIC PI. Multidrug resistance (*mdr1)* gene expression in adult acute leukemias: Correlations with treatment outcome and *in vitro* drug sensitivity. Blood 78: 586 - 592. **1991**.

MARIE JP, LEGRAND O. MDR1/P-gp expression as a prognostic factor in acute leukemias. *Advances in Experimental Medicine & Biology* 457: 1 – 9. **1999**

MARSH W, SICHERI D, CENTER MS. Isolation and characterization of adriamycin-resistant HL60 cells which are not defective in the initial intracellular accumulation of drug. *Cancer Research* 46: 4055 - 4057. **1986**.

MASCELLINO MT, IONA E, FATTORINI L, DE GREGORIS P, HU CQ, SANTORO C, OREFICI G. *In vitro* activity of clarithromycin alone or in combination with other micobacterial agents against *Mycobacterium avium-intracellulare* complex strains isolated from AIDS patients. *Journal of Chemotherapy* 3: 357-362. **1991**.

McPHAIL LC, CLAYTON CL, SNYDERMAN RA. A potential messenger role for unsaturated fatty acids: Activation of Ca^{2+}-dependent protein kinase. *Science* 224: 622-625. **1984**.

MECHETNER E, KYSHTOOBAYEVA A, ZONIS S, KIM H, STROUP R, GARCIA R, PARKER RJ, FRUEHAUF JP. Levels of multidrug resistance (MDR1) P-glycoprotein expression by human breast cancer correlate with *in vitro* resistance to taxol and doxorubicin. *Clinical Cancer Research* 4:389 – 398. **1998**.

MOORE VJ. A review of side-effects experienced by patients taking clofazimine. *Leprosy Review* 54: 327-335. **1983**.

MORROW CS, COWAN KH. Glutathion-S-transferases and drug resistance. *Cancer Cells* 2: 15 - 22. **1990**.

MOSSMAN T. Rapid colorimetric assay for cellular growth and survival: Applications to proliferation and cytotoxicity assays. *Journal of Immunological Methods* 65: 37-64. **1983**.

MYER MS, VAN RENSBURG CEJ. Chemosensitizing interactions of clofazimine and B669 with human K562 erythroleukaemia cells with varying levels of expression of P-glycoprotein. *Cancer Letter* 99: 73-78. **1996**.

NABORS MW, GRIFFIN CA, ZEHNBAUER BA, HRUBAN RH, PHILLIPS PC, GROSSMAN SA, BREM H, COLVIN OM. Multidrug resistance gene expression in human brain tumors. *Journal of Neurosurgery* 75: 941-946. **1991**.

NAITO M, TSURUO T. Functionally active homodimer of P-glycoprotein in multidrug-resistant tumor cells. *Biochemical & Biophysical Research Communications* 185: 284-290. **1992**.

NEBERT DW, NELSON DR, COON MJ, ESTABROOK RW, FEYEREISEN R, FUNJII-KURIYAMA Y, GOZALEZ FJ, GUENGERICH FP, GUNSALUS IC, JOHNSON EF. The P450 superfamily: Update on new sequences, gene mapping and recommended nomenclature. *DNA & Cell Biology* 10: 1-14. **1991**.

NOOTER K, HERWEIJER H. Multidrug resistance (mdr) genes in human cancer. *British Journal of Cancer* 63: 663-669. **1991**.

NUNBERG JH, KAUFMAN RJ, SCHIMKE RT, URLAUB G, CHASIN LA. Amplified dihydrofolate reductase genes are localized to a homogeneously staining region in a single chromosome in a methotrexate-resistant Chinese hamster ovary cell line. *Proceedings of the National Academy of Sciences of the of the United States of America* 75: 5553 - 5556. **1978**.

O'CONNOR R, O' SULLIVAN JF, O'KENNEDY R. The pharmacology, metabolism and chemistry of clofazimine. *Drug Metabolism Reviews* 27: 591-614. **1995**.

O'CONNOR R, O'SULLIVAN JF, O'KENNEDY R. Determination of serum and tissue levels of phenazines including clofazimine. *Journal of Chromatography B: Biomedical Applications* 681: 307 - 315. **1996**.

OISHI K, RAYNOR RL, CHARP PA, KUO JF. Regulation of protein kinase C by lysophopholipids: Potential role in signal transduction. *Journal of Biological Chemistry* 263: 6865-6871. **1988**.

OISHI K, ZHENG B, KUO JF. Inhibition of Na, K-ATPase and sodium pump by protein kinase C regulators sphingosine, lysophophatidylcholine and oleic acid. *Journal of Biological Chemistry* 265: 70-75. **1990**.

OKUDA K, OBATA H, NAKAJIMA Y, OHTSUKI T, OKAZAKI N, ONHISHI K. Prognosis of primary hepatocellular carcinoma. *Hepatology* 4: 3S-6S. **1984**.

PAJEVA IK, WIESE M, CORDES HP, SEYDEL JK. Membrane interactions of some catamphilic drugs and relation to their multidrug-resistance-reversing ability. *Journal of Cancer Research & Clinical Oncology* 122: 27 - 40. **1996**.

PALLARES-TRUJILLO J, LOPEZ-SORIANO FJ, ARGILES JM. Lipids: A key role in multidrug resistance? *International Journal of Oncology* 16(4): 783-798. **2000**

PARK GD. Pharmacokinetics. *In*: The scientific basis of clinical pharmacology: Principles and examples. Spector R, ed. Little, Brown and Company. Pp 67-12. **1986**.

PEARSON CK, CUNNINGHAM C. Multidrug resistance during cancer chemotherapy - biotechnological solutions to a clinical problem. *Trends in Biotechnology* 11: 511-516. **1993**.

PICHÉ A, GRIM J, RANCOURT C, GÓMEZ-NAVARRO J, REED JC, CURIEL DT. Modulation of Bcl-2 protein levels by an intracellular anti-Bcl-2 single-chain antibody increases drug-induced cytotoxicity in the breast cancer cell line MCF-7. *Cancer Research* 58: 2134-2140. **1998**.

PIRKER R, WALLNER J, GEISSLER K, LINKESH W, HAAS CA, BETTELHEIM P, HOPFNER M, SCHERRER R, VALENT P, HAVELEC L, *et al*. MDR1 gene expression and treatment outcome in acute myeloid leukemia. *Journal of the National Cancer Institute* 83: 708-712. **1991**.

PRATT WB, RUDDON RW, ENSMINGER WD, MAYBAUM J. The cancer problem. *In*: The anticancer drugs. Second edition. Oxford University Press. Pp 3-16. **1994a**.

PRATT WB, RUDDON RW, ENSMINGER WD, MAYBAUM J. Resistance to anticancer drugs. *In*: The anticancer drugs. Second edition. Oxford University Press. Pp 50 - 66. **1994b**.

RABINOVITCH PS, JUNE CH. Intracellular ionized calcium, membrane potential and pH. *In*: Flow cytometry: A clinical approach. Ormerod MG, ed. IRL Press, Oxford University Press. Pp 161-185. **1990**.

RAVIV Y, POLLARD HB, BRUGGEMANN EP, PASTAN I, GOTTESMAN MM. Photosensitized labeling of a functional multidrug transporter in living drug-resistant tumor cells. *Journal of Biological Chemistry* 265: 3975 - 3980. **1990.**

RAYMOND M, GROS P. Mammalian multidrug-resistance gene: Correlation of exon organization with structural domains and duplication of an ancestral gene. *Proceedings of the National Academy of Sciences of the United States of America* 86: 6488 - 6492. **1989**.

RAYMOND M, ROSE E, HOUSMAN D, GROS P. Physical mapping, amplification and overexpressing of the mouse *mdr* gene family in multidrug resistant cells. *Molecular & Cellular Biology* 10: 1642-1651. **1990**.

REED JC. BCL-2: prevention of apoptosis as a mechanism of drug resistance. *Hematology/Oncology Clinics of North America* 9: 451 - 473. **1995**.

RIORDAN JR, LING V. Purification of P-glycoprotein from plasma membrane vesicles of Chinese hamster ovary cell mutants with reduced colchicine permeability. *Journal of Biological Chemistry* 254: 12701 - 12705. **1979**.

RISCHIN D, LING V. Multidrug resistance in leukemia. *Cancer Treatment & Research* 64: 269- 293. **1993**.

RIVORY LP, AVENT KM, POND SM. Effects of lipophilicity and protein binding on the hepatocellular uptake and hepatic disposition of two anthracyclines, doxorubicin and iododoxorubicin. *Cancer Chemotherapy & Pharmacology* 38: 439-445. **1996**.

ROBINSON LJ, ROEPE PD. Effects on membrane potential versus pH_i on the cellular retention of doxorubicin analyzed via a comparison between cystic fibrosis transmembrane conductance regulator (CTR) and multidrug resistance (MDR) transfectants. *Biochemical Pharmacology* 52: 1081 - 1095. **1996**.

ROEPE PD. The role of the MDR protein in altered drug translocation across tumor cell membranes. *Biochimica et Biophysica Acta* 1241: 385-405. **1995**.

RUFF P, CHASEN MR, VAN RENSBURG CEJ. A phase II study of oral clofazimine in unresectable and metastatic hepatocellular carcinoma. *Annals of Oncology* 9: 217-219. **1998**.

SARKADI B, PRICE EM, BOUCHER RC, GERMANN UA, SCARBOROUGH GA. Expression of the human multidrug resistance cDNA in insect cells generates a high activity drug-stimulated membrane ATPase. *Journal of Biological Chemistry* 267: 4854 - 4858. **1992**.

SAVAGE JE, O'SULLIVAN JF, ZEIS BM, ANDERSON R. Investigation of structural properties of dihydrophenazines which contribute to their pro-oxidative interactions with human phagocytes. *Journal of Antimicrobial Chemotherapy* 23: 691-700. **1989**.

SCAGLIOTTI GV, NOVELLO S, SELVAGGI G. Multidrug resistance in non-small-cell lung cancer. *Annals of Oncology* 10 Suppl 5: S83 –86. **1999**

SCHEPER RJ, SCHEFFER GL, FLENS MJ, VAN DER VALK P, BROXTERMAN HJ, IZQUIERDO MA. Transporter molecules in multidrug resistance. *Cytotechnology* 19: 187 - 190. **1996**.

SCHINKEL AH. The physiological function of drug-transporting P-glycoproteins. *Seminars in Cancer Biology* 8: 161-170. **1997**.

SCHINKEL AH. Pharmacological insights from P-glycoprotein knockout mice. *International Journal of Clinical Pharmacology & Therapeutics* 36: 9-13. **1998**.

SCHLUESENER HJ, KOEPPEL C, JUNG S. Multidrug transport in human autoimmune T line cells and peripheral blood lymphocytes. *Immunopharmacology* 23: 37-48. **1992**.

SCHOENLEIN PV. Molecular cytogenetics of multiple drug resistance. *In*: Multiple drug resistance in cancer: Cellular, molecular and clinical approaches. (Reprinted from Cytotechnology, volume 12, 1993). Clynes M, ed. Kluwer Academic Publishers. Pp 63-89. **1994**.

SCHWARTZMANN G, CERSKI CT, SANDER E, SPRINZ E, KRONFELD M. P-glycoprotein expression in AIDS-related Kaposi's sarcoma. *Journal of the National Cancer Institute* 81: 1755 - 1756. **1989**.

SEHESTED M, SIMPSON D, SKOVSGAARD T, BUHL-JENSON P. Freeze-fracture study of plasma membranes in wild type and daunorubicin-resistanc Ehrlich ascites tumor and P388 leukemia cells. *Virchows Archiv. B. Cell Pathology Including Molecular Pathology* 56: 327-335. **1989**.

SHAPIRO HM. Cell membrane potential analysis. *In*: Methods of cell biology: Flow cytometry. Darzynkiewicz Z, Crissman HA, ed. Academic Press Inc. Pp 25-35. **1990**.

SHAPIRO AB, LING V. Using purified P-glycoprotein to understand multidrug resistance. *Journal of Bioenergetics & Biomembranes* 27: 7 - 13. **1995**.

SHAPIRO AB, FOX K, LEE P, YANG YD, LING V. Functional intracellular P-glycoprotein. *International Journal of Cancer* 76: 857 – 864. **1998.**

SHAROM FJ, LIU R, ROMSICKI Y, LU P. Insights into the structure and substrate interactions of the P-glycoprotein multidrug transporter from spectroscopic studies. *Biochimica et Biophysica Acta* 1461(2): 327 – 345. **1999.**

SIKIC BI, FISHER GA, LUM BL, HALSEY J, BEKETIC-ORESKOVIC L, CHEN G. Modulation and prevention of multidrug resistance by inhibitors of P-glycoprotein. *Cancer Chemotherapy & Pharmacology* 10(Supplement): S13 - S19. **1997**.

SINICROPE FA, DUDEJA PK, BISSONNETTE BM, SAFA AR, BRASITUS TA. Modulation of P-glycoprotein-mediated drug transport by alterations in lipid fluidity of rat liver canalicular membrane vesicles. *Journal of Biological Chemistry* 267: 24995-25002. **1992**.

SIROTNAK FM, YANG CH, MINES LS, ORIBE E, BIEDLER JL. Markedly altered membrane transport and intracellular binding of vincristine in multidrug-resistant Chinese hamster cells selected for resistance to vinca alkaloids. *Journal of Cellular Physiology* 126: 266 - 274. **1986**.

SKACH WR, CALAYAG MC, LINGAPPA VR. Evidence for an alternate model of human P-glycoprotein structure and biogenesis. *Journal of Biological Chemistry* 268: 6903-6908. **1993**.

SKOVSGAARD T. Mechanisms of resistance to daunorubicin in Ehrlich ascites tumor cells. *Cancer Research* 38: 1785 - 1791. **1978a**.

SKOVSGAARD T. Mechanism of cross-resistance between vincristine and daunomycin in Ehrlich ascites tumor cells. *Cancer Research* 38: 4722 - 4727. **1978b**.

SONNEVELD P, WIEMER E. Inhibitors of multidrug resistance. *Current Opinion in Oncology* 9: 543 - 548. **1997**.

SPEEG KV, DELEON C, McGUIRE WL. Uptake of the noncytotoxic transport probe prokainamide in the Chinese hamster ovary model of multidrug resistance. *Cancer Research* 52: 3539-3546. **1992**.

STAVROVSKAYA AA. Cellular mechanisms of multidrug resistance of tumor cells. Biochemistry (Moscow) 65(1): 95-106. **2000.**

SUGAWARA I, NAKAHAMA M, HAMADA H, TSURUO T, MORI S. Apparent stronger expression in the human adrenal cortex than in the human adrenal medulla of Mr 170,000 - 180,000 P-glycoprotein. *Cancer Research* 48: 4611-4614. **1988**.

TANNER MK, WELLHAUSEN SR. Flow cytometric detection of fluorescent redistributional dyes for measurement of cell transmembrane potential. *In*: Methods in molecular biology: Volume 91: Flow cytometric protocols. Jaroszeski MJ, Heller R, ed. Humana Press. Pp 85 - 95. **1998**.

TILLEMENT JP, HOUIN G, ZIN R, URIEN S, ALBENGRES E, BARRE J, LECOMTE M, D'ATHIS P, SEBILLE B. The binding of drugs to biological macromolecules in plasma. *Advances in Drug Research* 13: 59-94. **1984**.

TISHLER DM, WEINBERG KI, SENDER LS, NOLTA JA, RAFFEL C. Multidrug resistance gene expression in pediatric primitive neuroectodermal tumor of the central nervous system. *Journal of Neurosurgery* 76: 507-512. **1992**.

TSURUO T, IIDA H, TSUKAGOSHI S, SAKURAI Y. Overcoming of vincristine resistance in P388 leukemia *in vivo* and *in vitro* through enhanced cytotoxicity of vincristine and vinblastine by verapamil. *Cancer Research* 41: 1967-1972. **1981**.

TSURUO T. Circumvention of drug resistance with calcium channel blockers and monoclonal antibodies. *In*: Drug resistance in cancer therapy. Ozols RF, ed. Kluwer Academic Publishers. Pp 73-95. **1989**.

TWENTYMAN PR, FOX NE, WRIGHT KA, BLEEHEN NM. Derivation and preliminary characterisation of adriamycin resistant lines of human lung cancer cells. *British Journal of Cancer* 53: 529-537. **1986**.

TWENTYMAN PR, WRIGHT KA, WALLACE HM. Effects of cyclosporin A and a non-immunosuppressive analogue, O-acetyl cyclosporin A, upon the growth of parent and multidrug resistant human lung cancer cells *in vitro*. *British Journal of Cancer* 65: 335-340. **1992**.

TWENTYMAN PR. Transport proteins in drug resistance: Biology and approaches to circumvention. *Journal of Internal Medicine. Supplement.*740: 133-137. **1997**.

UEDA K, OKAMURA N, HIRAI M, TANIGAWARA Y, SAEKI T, KIOKA N, KOMANO T, HORI R. Human P-glycoprotein transports cortisol, aldosterone, and dexamethasone, but not progesterone. *Journal of Biological Chemistry* 267: 24248-24252. **1992**.

VAN DEN HEUVEL-EIBRINK MM, SONNEVELD P, PIETERS R. The prognostic significance of membrane transport-associated multidrug resistance (MDR) proteins in leukemia. *International Journal of Clinical Pharmacology & Therapeutics* 38(3):94-110. **2000**

VAN DER BLIEK AM, BAAS F, VAN DER VELDE-KOERTS T, BIEDLERS JL, MEYERS MB, OZOLS RF, HAMILTON TC, JOENJE H, BORST P. Genes amplified and overexpressed in human multidrug-resistant cell lines. *Cancer Research* 48: 5927-5932. **1988**.

VAN RENSBURG CEJ, VAN STADEN AM, ANDERSON R. The riminophenazine agents clofazimine and B669 inhibit the proliferation of cancer cell lines *in vitro* by phopholipase A_2-mediated oxidative and non-oxidative mechanisms. *Cancer Research* 53: 318-323. **1993a**.

VAN RENSBURG CEJ, DURANDT C, GARLINSKI PJ, O'SULLIVAN JF. Evaluation of the antineoplastic activities of the riminophenazine agents clofazimine and B669 in tumor-bearing rats and mice. *International Journal of Oncology* 3: 1011-1013. **1993b**.

VAN RENSBURG CEJ, ANDERSON R, MYER MS, JOONE GK, O'SULLIVAN JF. The riminophenzine agents clofazimine and B669 reverse acquired multidrug resistance in a human lung cancer cell line. *Cancer Letters* 85: 59-63. **1994**.

VAN RENSBURG CEJ, THERON AJ, CHASEN M. The riminophenazine agents clofazimine and B669 inhibit the proliferation of intrinsically multidrug resistant carcinoma cell lines. *Oncology Report* 3: 103-106. **1996**.

VAN RENSBURG CEJ, ANDERSON R, O'SULLIVAN JF. Riminophenazine compounds: Pharmacology and anti-neoplastic potential. *Critical Reviews in Oncology/Hematology* 25: 55-67. **1997**.

VOET D, VOET JC. Lipid metabolism. *In*: Biochemistry. Second edition. John Wiley & Sons. Pp 662-728. **1995a**.

VOET D, VOET JC. Lipids and membranes. *In*: Biochemistry. Second edition. John Wiley & Sons. Pp 277-329. **1995b**.

VOET D, VOET JC. Transport through membranes. *In*: Biochemistry. Second edition. John Wiley & Sons. Pp 513-537. **1995c**.

VOET D, VOET JC. Life. *In*: Biochemisty. Second edition. John Wiley & Sons, Inc. Pp 2-28. **1995d**.

WADKINS RM, ROEPE PD. Biophysical aspects of P-glycoprotein-mediated multidrug resistance. *Internal Review of Cytology* 171: 121 - 165. **1997**.

WALKER JE, SARASTE M, RUNSWICK MJ, GAY NJ. Distantly related sequences in the a and b subunits of ATP synthetase, myosin, kinases and other ATP-requiring enzymes and a common nucleotide binding fold. *EMBO Journal* 1: 945 - 951. **1982**.

WEISS SJ, SLIVKA A. Monocytes and granulocytes-mediated tumor cell destruction. *Journal of Clinical Investigations* 69: 255-262. **1982**.

WOLF DC, HORWITZ SB. P-glycoprotein transports corticosterone and is photoaffinity-labeled by the steroid. *International Journal of Cancer* 52: 141-146. **1992**.

WORLD HEALTH ORGANIZATION. Weekly Epidemiological Report 62: 101-108. **1987**.

WRIGHT LC, DYNE M, HOLMES KT, MOUNTFORD CE. Phospholipid content and ether linked phospholipid content alter with cellular resistance to vinblastine. *Biochemical & Biophysical Research Communications* 133: 539-545. **1985**.

YAWALKAR SJ, VISCHER W. Lamprene (clofazimine) in leprosy. *Leprosy Review* 50: 135-144. **1979**.

YOUNG RC. Drug resistance: The clinical problem. *In*: Drug resistance in cancer therapy. Ozols RF, ed. Kluwer Academic Publishers. Pp 1-12. **1989**.

ZEIS BM, ANDERSON R. Clofazimine-mediated stimulation of prostaglandin synthesis and free radical production as a novel mechanism of drug-induced immunosupression. *International Journal of Immunopharmacology* 8: 731-739. **1986**.

ZHANG J-T, LING V. Study of membrane orientation and glycosylated extracellular loops of mouse P-glycoprotein by *in vivo* translation. *Journal of Biological Chemistry* 266: 18224 - 18232. **1991**.

ZHANG J-T, DUTHIE M, LING V. Membrane topology on the N-termianl half of the hamster P-glycoprotein molecule. *Journal of Biological Chemistry* 268: 15101-15110. **1993**.

ADDENDUM A

PEARSON KORRELASIES

1. Doelwit

In hierdie byvoegsel is die verskillende eksperimentele bepalings met mekaar vergelyk, om uit te vind tot watter mate die veranderlikes in een bepaling die veranderlikes in die ander bepalings beïnvloed het.

2. Inleiding

Die korrelasie koeffisiënt (r) word gebruik om die verband tussen twee reekse veranderlikes te bepaal. Die rigting en grootte van die korrelasie tussen die twee reekse veranderlikes word deur *r* gekwantifiseer **[Johnson, 1988; Freund & Simon, 1995]**.

Die waarde van r varieer tussen -1.0 en 1.0. Indien r = 0 is, dui dit daarop dat daar geen korrelasie tussen die veranderlikes, waargeneem is nie. Indien r 'n positiewe waarde besit, dui dit daarop dat die twee veranderlikes wat met mekaar vergelyk word, gesamentlik toeneem of afneem. Indien r = +1.0 is, dui dit daarop dat die data 'n perfekte reguit lyn, met 'n opwaartse (positiewe helling), vorm. Daarenteen dui r = -1.0 daarop dat die data 'n perfekte reguit lyn, met 'n afwaartse (negatiewe) helling, vorm. 'n Negatiewe waarde van r dui daarop dat die een veranderlike toegeneem het, terwyl die ander veranderlike afgeneem het **[Johnson, 1988; Freund & Simon, 1995]**. Afhangende van die waarde van r, kan die korrelasie tussen twee reekse veranderlikes as 'n sterk korrelasie, matige korrelasie of swak korrelasie geïnterpreteer word. Dit is egter 'n baie objektiewe wyse van interpretering. Verder beteken 'n betekenisvolle r-waarde nie noodwendig dat die data wat met mekaar vergelyk is, linieêr met mekaar korreleer nie **[Freund & Simon, 1995]**.

Die verband (korrelasie) tussen twee veranderlikes kan meer duidelik gekwantifiseer word, indien die r^2 bepaal word. Dit staan as die koeffisiënt van bepaling ("correlation of determination") bekend. Die waarde van r^2 wissel tussen 0 en 1 en dui die sterkte van die

linieëre korrelasie tussen die veranderlikes aan **[Johnson, 1988]**. Byvoorbeeld, indien $r^2 = 0.59$ is, dui dit daarop dat 59% van die variasie in die een veranderlike (X) direk linieër verband hou met die waargeneemde variasie van die tweede veranderlike (Y) of dat 59% van die variasie in Y direk linieër verband hou met die waargeneemde variasie in X **[Freund & Simon, 1995]**.

In hierdie addendum is die koeffisiënt van bepaling (r^2-waarde) in tabel vorm opgesom. Die r^2-waardes is in drie groepe verdeel, naamlik sterk korrelasies ($r^2 \geq 0.8$), matige korrelasies ($0.8 > r^2 \geq 0.6$) en swak korrelasies ($0.6 > r^2 \geq 0.4$). Die ooreenstemmende r-waarde is in hakies onder elk van bogenoemde r^2-waardes aangedui. Hierdie r-waarde toon of 'n positiewe of negatiewe korrelasie waargeneem is. Om interpretering van die resultate te vergemaklik, is bogenoemde drie groepe korrelasies as volg in die tabelle aangedui. Die p-waarde sowel as die aantal punte wat met mekaar gekorreleer is, is ook in die tabel aangedui.

$r^2 \geq 0.8$
$0.8 > r^2 \geq 0.6$
$0.6 > r^2 \geq 0.4$
$r^2 < 0.4$

3. Resultate

3.1. Pearson korrelasies tussen die verskillende eksperimentele bepalings wat met die geneesmiddel-sensitiewe H69/P selle gedoen is

Tabel 1A: Pearson korrelasies tussen verskillende eksperimentele bepalings gedoen op geneesmiddel-sensitiewe H69/P selle

		7-DAE MTT BEPALING	
		DIREKTE SITOTOKSISITEIT (IK_{50})	SENSITISERINGS VERMOË VIR VINBLASTIEN (IK_{50})
7-DAE MTT BEPALING	DIREKTE SITOTOKSISITEIT (IK_{50})	-	**$r^2 = 0.6$** ($r = 0.7$) ($p = 0.25$) ($n = 4$)
	SENSITISERINGS VERMOË VIR VINBLASTIEN (IK_{50})	**$r^2 = 0.6$** ($r = 0.7$) ($p = 0.25$) ($n = 4$)	-
[^{3}H]VINBLASTIEN OPNAME BEPALING	1.0 µg/ml	$r^2 = 0.0$	$r^2 = 0.0$
TIAZOOL ORANJE OPNAME BEPALING	1.25 µg/ml	**$r^2 = 0.9$** ($r = 0.9$) ($p = 0.05$) ($n = 4$)	**$r^2 = 0.6$** ($r = 0.8$) ($p = 0.22$) ($n = 4$)

Tabel 11.1A vervolg . . .

Tabel 11.1A vervolg . . .

		7-DAE MTT BEPALING	
		DIREKTE SITOTOKSISITEIT (IK_{50})	**SENSITISERINGS VERMOË VIR VINBLASTIEN (IK_{50})**
INHIBISIE VAN KALIUM OPNAME	**2.5 µg/ml**	**$r^2 = 0.4$** (r = -0.6) (p = 0.40) (n = 4)	$r^2 = 0.0$
	5.0 µg/ml	**$r^2 = 0.4$** (r = -0.6) (p = 0.36) (n = 4)	$r^2 = 0.2$
	10.0 µg/ml	$r^2 = 0.0$	$r^2 = 0.0$
VERANDERINGS IN MEMBRAAN POTENSIAAL	**1.25 µg/ml**	$r^2 = 0.0$	**$r^2 = 0.4$** (r = 0.6) (p = 0.42) (n = 4)
	2.5 µg/ml	$r^2 = 0.0$	**$r^2 = 0.6$** (r = 0.8) (p = 0.22) (n = 4)
LIPOFILISITEIT (PARTISSIE KOEFFISIËNTE)		$r^2 = 0.1$	$r^2 = 0.0$
***IN VITRO* AKKUMULERING VAN RIMINOFENASIEN VERBINDINGS**		$r^2 = 0.3$	$r^2 = 0.0$
HEMOLISE VAN SKAAP ROOIBLOEDSELLE	**5 µg/ml**	**$r^2 = 0.1$** (r = 1.0) (p = 0.002) (n = 4)	$r^2 = 0.0$
	10 µg/ml	$r^2 = 0.2$	$r^2 = 0.1$

Tabel 1B: Pearson korrelasies tussen verskillende eksperimentele bepalings gedoen op geneesmiddel-sensitiewe H69/P selle

		[^{3}H]VINBLASTIEN OPNAME BEPALING (1.0 µg/ml)	TIAZOOL ORANJE OPNAME BEPALING (1.25 µg/ml)
[^{3}H]VINBLASTIEN OPNAME BEPALING	1.0 µg/ml	-	$r^2 = 0.0$
TIAZOOL ORANJE OPNAME BEPALING	1.25 µg/ml	$r^2 = 0.0$	-
INHIBISIE VAN KALIUM OPNAME	2.50 µg/ml	$r^2 = 0.2$	$r^2 = 0.1$
	5.0 µg/ml	**$r^2 = 0.6$** (r = 0.8) (p = 0.22) (n = 4)	$r^2 = 0.1$
	10.0 µg/ml	**$r^2 = 0.9$** (r = 0.9) (p = 0.06) (n = 4)	$r^2 = 0.0$
VERANDERINGS IN MEMBRAAN POTENSIAAL	1.25 µg/ml	**$r^2 = 0.4$** (r = 0.6) (p = 0.40) (n = 4)	$r^2 = 0.0$
	2.50 µg/ml	$r^2 = 0.3$	$r^2 = 0.1$
LIPOFILISITEIT (PARTISSIE KOEFFISIËNTE)		**$r^2 = 0.7$** (r = 0.8) (p = 0.19) (n = 4)	$r^2 = 0.2$
IN VITRO AKKUMULERING VAN RIMINOFENASIEN VERBINDINGS		$r^2 = 0.3$	$r^2 = 0.1$

Tabel 11.1B vervolg . . .

Tabel 11.1B vervolg . . .

		[^{3}H]VINBLASTIEN OPNAME BEPALING (1.0 µg/ml)	TIAZOOL ORANJE OPNAME BEPALING (1.25 µg/ml)
HEMOLISE VAN SKAAP ROOIBLOEDSELLE	5 µg/ml	$r^2 = 0.0$	**$r^2 = 0.9$** (r = 0.9) (p = 0.04) (n = 4)
	10 µg/ml	**$r^2 = 0.4$** (r = 0.7) (p = 0.33) (n = 4)	$r^2 = 0.0$

Tabel 1C: Pearson korrelasies tussen verskillende eksperimentele bepalings gedoen op geneesmiddel-sensitiewe H69/P selle

		INHIBISIE VAN KALIUM OPNAME			VERANDERINGS IN MEMBRAAN POTENSIAAL	
		2.5 µg/ml	5.0 µg/ml	10.0 µg/ml	1.25 µg/ml	2.5 µg/ml
INHIBISIE VAN KALIUM OPNAME	2.5 µg/ml	-	-	-	**$r^2 = 0.6$** (r = 0.8) (p = 0.23) (n = 4)	**$r^2 = 0.7$** (r = 0.8) (p = 0.14) (n = 4)
	5.0 µg/ml	-	-	-	$r^2 = 0.3$	**$r^2 = 0.4$** (r = 0.6) (p = 0.36) (n= 4)
	10.0 µg/ml	-	-	-	**$r^2 = 0.6$** (r = 0.8) (p = 0.20) (n = 4)	**$r^2 = 0.7$** (r = 0.8) (p = 0.16) (n = 4)
VERANDERINGS IN MEMBRAAN POTENSIAAL	1.25 µg/ml	**$r^2 = 0.6$** (r = 0.8) (p = 0.23) (n = 4)	$r^2 = 0.3$	**$r^2 = 0.6$** (r = 0.8) (p = 0.20) (n = 4)	-	-
	2.50 µg/ml	**$r^2 = 0.7$** (r = 0.8) (p = 0.14) (n = 4)	**$r^2 = 0.4$** (r = 0.6) (p = 0.36) (n= 4)	**$r^2 = 0.7$** (r = 0.8) (p = 0.16) (n = 4)	-	-
LIPOFILISITEIT (PARTISSIE KOEFFISIËNTE)		$r^2 = 0.0$	$r^2 = 0.1$	$r^2 = 0.3$	$r^2 = 0.0$	$r^2 = 0.0$
IN VITRO AKKUMULERING VAN RIMINOFENASIEN VERBINDINGS		**$r^2 = 1.0$** (r = 1.0) (p = 0.01) (n = 4)	**$r^2 = 0.7$** (r = 0.9) (p = 0.14) (n = 4)	**$r^2 = 0.6$** (r = 0.8) (p = 0.21) (n = 4)	**$r^2 = 0.6$** (r = 0.8) (p = 0.21) (n = 4)	**$r^2 = 0.8$** (r = 0.9) (p = 0.12) (n = 4)

Tabel 11.1C vervolg . . .

Tabel 11.1C vervolg . . .

		INHIBISIE VAN KALIUM OPNAME			VERANDERINGS IN MEMBRAAN POTENSIAAL	
		2.5 µg/ml	5.0 µg/ml	10.0 µg/ml	1.25 µg/ml	2.5 µg/ml
HEMOLISE VAN SKAAP ROOIBLOEDSELLE	5 µg/ml	**$r^2 = 0.4$** (r = - 0.6) (p = 0.39) (n = 4)	**$r^2 = 0.4$** (r = - 0.6) (p = 0.39) (n = 4)	$r^2 = 0.0$	$r^2 = 0.0$	$r^2 = 0.0$
	10 µg/ml	**$r^2 = 0.9$** (r = 1.0) (p = 0.04) (n = 4)	**$r^2 = 0.8$** (r = 0.9) (p = 0.11) (n = 4)	**$r^2 = 0.8$** (r = 0.9) (p = 0.13) (n = 4)	**$r^2 = 0.7$** (r = 0.8) (p = 0.17) (n = 4)	**$R^2 = 0.8$** (r = 0.9) (p= 0.09) (n = 4)

Tabel 1D: Pearson korrelasies tussen verskillende eksperimentele bepalings gedoen op geneesmiddel-sensitiewe H69/P selle

		LIPOFILISITEIT (PARTISSIE KOEFFISIËNTE)	*IN VITRO* AKKUMULERING VAN RIMINOFENASIEN VERBINDINGS
LIPOFILISITEIT (PARTISSIE KOEFFISIËNTE)		-	$r^2 = 0.0$
IN VITRO AKKUMULERING VAN RIMINOFENASIEN VERBINDINGS		$r^2 = 0.0$	-
HEMOLISE VAN SKAAP ROOIBLOED-SELLE	5 µg/ml	$r^2 = 0.2$	$r^2 = 0.3$
	10 µg/ml	$r^2 = 0.0$	**$r^2 = 1.0$** (r = 1.0) (p = 0.01) (n = 4)

3.2. Pearson korrelasies tussen die verskillende eksperimentele bepalings wat met die veelvuldige geneesmiddel weerstandbiedende H69/LX4 selle gedoen is

Tabel 2A: Pearson korrelasies tussen verskillende eksperimentele bepalings gedoen op veelvuldige geneesmiddel weerstandbiedende H69/LX4 selle

		7-DAE MTT BEPALING	
		DIREKTE SITOTOKSISITEIT (IK_{50})	SENSITISERINGS VERMOË VIR VINBLASTIEN (IK_{50})
7-DAE MTT BEPALING	DIREKTE SITOTOKSISITEIT (IK_{50})	-	**$r^2 = 0.6$** (r = 0.8) (P = 0.25) (n = 4)
	SENSITISERINGS VERMOË VIR VINBLASTIEN (IK_{50})	**$r^2 = 0.6$** (r = 0.8) (p = 0.25) (n = 4)	-
[^{3}H]VINBLASTIEN OPNAME BEPALING	1.0 µg/ml	**$r^2 = 0.6$** (r = -0.8) (p = 0.22) (n = 4)	**$r^2 = 0.7$** (r = -0.8) (p = 0.17) (n = 4)
TIAZOOL ORANJE OPNAME BEPALING	1.25 µg/ml	**$r^2 = 0.4$** (r = -0.6) (p = 0.38) (n = 4)	**$r^2 = 0.7$** (r = -0.8) (p = 0.19) (n = 4)

Tabel 11.2A vervolg . . .

Tabel 11.2A vervolg . . .

		7-DAE MTT BEPALING	
		DIREKTE SITOTOKSISITET (IK_{50})	**SENSITISERINGS VERMOË VIR VINBLASTIEN (IK_{50})**
INHIBISIE VAN KALIUM OPNAME	0.6 µg/ml	**$r^2 = 0.6$** (r = 0.8) (p = 0.24) (n = 4)	**$r^2 = 1.0$** (r = 1.0) (p = 0.02) (n = 4)
	1.25 µg/ml	$r^2 = 0.1$	$r^2 = 0.1$
VERANDERINGS IN MEMBRAAN POTENSIAAL	1.25 µg/ml	**$r^2 = 0.4$** (r = 0.6) (p = 0.40) (n = 4)	**$r^2 = 1.0$** (r = 1.0) (p = 0.02) (n = 4)
	2.5 µg/ml	**$r^2 = 0.5$** (r = 0.7) (p = 0.29) (n = 4)	**$r^2 = 1.0$** (r = 1.0) (p = 0.01) (n = 4)
LIPOFILISITEIT (PARTISSIE KOEFFISIËNTE)		$r^2 = 0.1$	$r^2 = 0.1$
***IN VITRO* AKKUMULERING VAN RIMINOFENASIEN VERBINDINGS**		$r^2 = 0.2$	**$r^2 = 0.5$** (r = -0.7) (p = 0.28) (n = 4)
HEMOLISE VAN SKAAP ROOIBLOEDSELLE	5 µg/ml	**$r^2 = 1.0$** (r = 1.0) (p = 0.02) (n = 4)	**$r^2 = 0.7$** (r = -0.8) (p = 0.18) (n = 4)
	10 µg/ml	$r^2 = 0.1$	**$r^2 = 0.8$** (r = -0.9) (p = 0.08) (n = 4)

Tabel 2B: Pearson korrelasies tussen verskillende eksperimentele bepalings gedoen op veelvuldige geneesmiddel weerstandbiedende H69/LX4 selle

		[^{3}H]VINBLASTIEN OPNAME BEPALING (1.0 µg/ml)	TIAZOOL ORANJE OPANME BEPALING (1.25 µg/ml)
[^{3}H]VINBLASTIEN OPNAME BEPALING	1.0 µg/ml	-	$r^2 = 0.1$
TIAZOOL ORANJE OPANAME BEPALING	1.25 µg/ml	$r^2 = 0.1$	-
INHIBISIE VAN KALIUM OPNAME	0.6 µg/ml	**$r^2 = 0.5$** (r = - 0.7) (p = 0.11) (n = 4)	**$r^2 = 0.8$** (r = - 0.9) (p = 0.08 (n = 4)
	1.25 µg/ml	$r^2 = 0.2$	$r^2 = 0.3$
VERANDERINGS IN MEMBRAAN POTENSIAAL	1.25 µg/ml	**$r^2 = 0.5$** (r = - 0.7) (p = 0.27) (n = 4)	**$r^2 = 0.7$** (r = - 0.8) (p = 0.17 (n = 4)
	2.5 µg/ml	**$r^2 = 0.8$** (r = - 0.9) (p = 0.11) (n = 4)	**$r^2 = 0.5$** (r = - 0.7) (p = 0.0.29) (n = 4)
LIPOFILISITEIT (PARTISSIE KOEFFISIËNTE)		$r^2 = 0.1$	$r^2 = 0.0$
IN VITRO AKKUMULERING VAN RIMINOFENASIEN VERBINDINGS		$r^2 = 0.0$	**$r^2 = 0.8$** (r = 0.9) (p = 0.08) (n = 4)
HEMOLISE VAN SKAAP ROOIBLOEDSELLE	5 µg/ml	**$r^2 = 0.5$** (r = - 0.7) (p = 0.31) (n = 4)	**$r^2 = 0.6$** (r = - 0.8) (p = 0.24) (n = 4)
	10 µg/ml	$r^2 = 0.0$	**$r^2 = 0.9$** (r = 0.9) (p = 0.07) (n = 4)

Tabel 2C: Pearson korrelasies tussen verskillende eksperimentele bepalings gedoen op veelvuldige geneesmiddel weerstandbiedende H69/LX4 selle

		INHIBISIE VAN KALIUM OPNAME	
		0.6 µg/ml	1.25 µg/ml
INHIBISIE VAN KALIUM OPNAME	0.6 µg/ml	-	-
	1.25 µg/ml	-	-
VERANDERINGS IN MEMBRAAN POTENSIAAL	1.25 µg/ml	**$r^2 = 0.9$** (r = 1.0) (p = 0.04) (n = 4)	$r^2 = 0.1$
	2.5 µg/ml	**$r^2 = 0.9$** (r = 0.9) (p = 0.07) (n = 4)	$r^2 = 0.0$
LIPOFILISITEIT (PARTISSIE KOEFFISIËNTE)		$r^2 = 0.0$	$r^2 = 0.0$
IN VITRO AKKUMULERING VAN RIMINOFENASIEN VERBINDINGS		**$r^2 = 0.5$** (r = - 0.7) (p = 0.32) (n = 4)	**$r^2 = 0.4$** (r = 0.7) (p = 0.33) (n = 4)
HEMOLISE VAN SKAAP ROOIBLOEDSELLE	5 µg/ml	**$r^2 = 0.7$** (r = 0.8) (p = 0.17) (n = 4)	$r^2 = 0.0$
	10 µg/ml	**$r^2 = 0.7$** (r = - 0.8) (p = 0.18) (n = 4)	**$r^2 = 0.6$** (r = 0.8) (p = 0.23) (n = 4)

Tabel 2D: Pearson korrelasies tussen verskillende eksperimentele bepalings gedoen op veelvuldige geneesmiddel weerstandbiedende H69/LX4 selle

		VERANDERINGS IN MEMBRAAN POTENSIAAL		LIPOFILISITEIT (PARTISSIE KOEFFISIËNTE)	*IN VITRO* AKKUMULERING VAN RIMINOFENASIEN VERBINDINGS
		1.25 µg/ml	2.50 µg/ml		
VERANDERINGS IN MEMBRAAN POTENSIAAL	1.25 µg/ml	-	-	$r^2 = 0.1$	$r^2 = 0.3$
	2.5 µg/ml	-	-	$r^2 = 0.1$	$r^2 = 0.1$
LIPOFILISITEIT (PARTISSIE KOEFFISIËNTE)		$r^2 = 0.1$	$r^2 = 0.1$	-	$r^2 = 0.1$
IN VITRO AKKUMULERING VAN RIMINOFENASIEN VERBINDINGS		$r^2 = 0.3$	$r^2 = 0.1$	$r^2 = 0.1$	-
HEMOLISE VAN SKAAP ROOIBLOEDSELLE	5 µg/ml	**$r^2 = 0.4$** ($r = 0.7$) ($p = 0.34$) ($n = 4$)	**$r^2 = 0.5$** ($r = 0.7$) ($p = 0.29$) ($n = 4$)	$r^2 = 0.2$	**$r^2 = 0.4$** ($r = -0.6$) ($p = 0.40$) ($n = 4$)
	10 µg/ml	**$r^2 = 0.7$** ($r = -0.8$) ($p = 0.19$) ($n = 4$)	**$r^2 = 0.4$** ($r = -0.6$) ($p = 0.37$) ($n = 4$)	$r^2 = 0.0$	**$r^2 = 0.8$** ($r = 0.9$) ($p = 0.13$) ($n = 4$)

3.3. Pearson korrelasies tussen verkeie eksperimentele bepalings en die riminofenasien-geïnduseerde inhibisie van tumor groei, riminofenasien tumorvlakke sowel as die riminofenasien serum vlakke waargeneem tydens *in vivo* studies met eksperimentele rotte

Tabel 3: Pearson korrelasies tussen verskillende eksperimentele bepalings en die riminofenasien-geïnduseerde inhibisie van tumor groei, riminofenasien tumorvlakke sowel as riminofenasien serumvlakke

		RIMINOFENASIEN-GEÏNDUSEERDE INHIBISIE VAN TUMOR GROEI	*IN VIVO* TUMORVLAKKE	*IN VIVO* SERUMVLAKKE
IN VITRO SITOTOKSISITEIT	H69/P sellyn	$r^2 = 0.0$	**$r^2 = 0.7$** (r = 0.8) (p = 0.19) (n = 4)	**$r^2 = 0.8$** (r = 0.9) (p = 0.10) (n = 4)
	H69/LX4 sellyn	$r^2 = 0.1$	**$r^2 = 0.7$** (r = 0.9) (p = 0.13) (n = 4)	**$r^2 = 0.9$** (r = 0.9) (p = 0.06) (n = 4)
RIMINOFENASIEN-GEÏNDUSEERDE INHIBISIE VAN TUMOR GROEI		-	$r^2 = 0.3$	$r^2 = 0.2$
IN VIVO SERUMVLAKKE		$r^2 = 0.2$	**$r^2 = 1.0$** (r = 1.0) (p = 0.02) (n = 4)	-

Tabel 3 vervolg . . .

Tabel 3 vervolg . . .

		RIMINOFENASIEN-GEÏNDUSEERDE INHIBISIE VAN TUMOR GROEI	*IN VIVO* TUMORVLAKKE	*IN VIVO* SERUMVLAKKE
LIPOFILISITEIT (PARTISSIE KOEFFISIËNTE)		$r^2 = 0.0$	$r^2 = 0.0$	$r^2 = 0.0$
IN VITRO AKKUMULERING VAN RIMINOFENASIEN VERBINDINGS		**$r^2 = 0.5$** ($r = 0.7$) ($p = 0.30$) ($n = 4$)	$r^2 = 0.0$	$r^2 = 0.1$
HEMOLISE VAN SKAAP ROOIBLOEDSELLE	5 µg/ml	$r^2 = 0.0$	$r^2 = 0.1$	**$r^2 = 0.8$** ($r = 0.9$) ($p = 0.13$) ($n = 4$)
	10 µg/ml	**$r^2 = 0.5$** ($r = 0.7$) ($p = 0.28$) ($n = 4$)	**$r^2 = 0.5$** ($r = 0.7$) ($p = 0.31$) ($n = 4$)	$r^2 = 0.0$

4. Samevatting

Die eksperimentele bepalings wat sterk korrelasies ($0.8 \leq r^2 \leq 1.0$) met mekaar getoon het, kan as volg opgesom word:

4.1. *In vitro* studies met H69/P selle

Die direkte *in vitro* sitotoksisiteit van die eksperimentele riminofenasien verbindings het met die riminofenasien-bemiddelde opname van tiazool oranje sowel as hemolise van skaap rooibloedselle, gekorreleer.

Die vermoë van die riminofenasien verbindings om die H69/P sellyn vir vinblastien te sensitiseer het met die vermoë van die verbindings om die selle vir doksorubisien te

sensitiseer, riminofenasien-bemiddelde [^{3}H]vinblastien opname sowel as die lipofilisiteit van die verbindings, gekorreleer.

Die riminofenasien-bemiddelde opname van [^{3}H]vinblastien het met die riminofenasien-bemiddelde inhibisie van kalium opname, die lipofilisiteit van die eksperimentele riminofenasien verbindings, die riminofenasien-geïnduseerde veranderings in die membraan potensiaal, die *in vitro* akkumulering van die verbindings sowel as die riminofenasien-geïnduseerde hemolise van skaap rooibloedselle, gekorreleer.

Die opname van tiazool oranje in die teenwoordigheid van die eksperimentele riminofenasien verbindings het met die riminofenasien-geïnduseerde veranderings in die membraan potensiaal gekorreleer.

Riminofenasien-bemiddelde inhibisie van kalium opname het met riminofenasien-geïnduseerde veranderings in die membraan potensiaal, *in vitro* akkumulering van die riminofenasien verbindings sowel as riminofenasien-geïnduseerde hemolise van skaap rooibloedselle gekorreleer.

Riminofenasien-geïnduseerde veranderings in membraan potensiale het met die *in vitro* akkumulering van die eksperimentele riminofenasien verbindings sowel as riminofenasien-geïnduseerde hemolise van skaap rooibloedselle gekorreleer.

Die *in vitro* akkumulering van riminofenasien verbindings het met die riminofenasien-geïnduseerde hemolise van skaap rooibloedselle, gekorreleer.

4.2. *In vitro* studies met H69/LX4 selle

Die direkte *in vitro* sitotoksisiteit van die eksperimentele riminofenasien verbindings het met die vermoë van die riminofenasien verbindings om die H69/LX4 sellyn vir doksorubisien te sensitiseer, die riminofenasien-bemiddelde opname van [^{3}H]vinblastien, riminofenasien-geïnduseerde inhibisie van kalium opname,

riminofenasien-geïnduseerde veranderings in die membraan potensiaal sowel as riminofenasien-bemiddelde hemolise van skaap rooibloedselle, gekorreleer.

Die vermoë van die riminofenasien verbindings om die H69/P sellyn vir vinblastien te sensitiseer het met die vermoë van die verbindings om die selle vir doksorubisien te sensitiseer sowel as die lipofilisiteit van die verbindings gekorreleer.

Die vermoë van die riminofenasien verbindings om die selle vir doksorubisien te sensitiseer het met die opname van [^{3}H]vinblastien in die teenwoordigheid van die riminofenasien verbindings gekorreleer.

Die riminofenasien-bemiddelde opname van [^{3}H]vinblastien het met die riminofenasien-bemiddelde inhibisie van kalium opname, die riminofenasien-geïnduseerde veranderings in die membraan potensiale sowel as die riminofenasien-geïnduseerde hemolise van skaap rooibloedselle, gekorreleer.

Die opname van tiazool oranje in die teenwoordigheid van die eksperimentele riminofenasien verbindings het met die riminofenasien-geïnduseerde veranderings in die membraan potensiaal, die *in vitro* akkumulering van die verbindings, sowel as die vermoë van die verbindings om skaap rooibloedselle te liseer, gekorreleer.

Riminofenasien-bemiddelde inhibisie van kalium opname het met riminofenasien-geïnduseerde veranderings in die membraan potensiaal, *in vitro* akkumulering van die riminofenasien verbindings sowel as riminofenasien-geïnduseerde hemolise van skaap rooibloedselle, gekorreleer.

Riminofenasien-geïnduseerde veranderings in membraan potensiale het met die riminofenasien-geïnduseerde hemolise van skaap rooibloedselle, gekorreleer.

Die *in vitro* akkumulering van riminofenasien verbindings het met die riminofenasien-geïnduseerde hemolise van skaap rooibloedselle, gekorreleer.

4.3. *In vivo* studies

Die riminofenasien-geïnduseerde inhibisie van tumor groei het met die *in vitro* akkumulering van die eksperimentele riminofenasien verbindings sowel as die riminofenasien-bemiddelde hemolise van skaap rooibloedselle, gekorreleer.

Die riminofenasien vlakke wat in die tumore waargeneem is, het met die direkte *in vitro* sitotoksisiteit, die riminofenasien vlakke in die serum sowel as die riminofenasien-bemiddelde hemolise van skaap rooibloedselle, gekorreleer.

Die riminofenasien vlakke in die serum, het met die direkte *in vitro* sitotoksisiteit, sowel as die riminofenasien-bemiddelde hemolise van skaap rooibloedselle, gekorreleer.