

BIBLIOGRAPHY

- Aggarwal BB, Bhardwaj A, Aggarwal RS, Seeram NP, Shishodia S, Takada Y. Role of resveratrol in prevention and therapy of cancer: preclinical and clinical studies. *Anticancer Res.* 2004; 24(5A):2783-840. Review. PubMed PMID: 15517885.
- Ai Z, Lu Y, Qiu S, Fan Z. Overcoming cisplatin resistance of ovarian cancer cells by targeting HIF-1-regulated cancer metabolism. *Cancer Lett* 2016; 373: 36–44.
- Ajduković J. HIF-1 — a big chapter in the cancer tale. *Exp Oncol.* 2016; 38(1):9-12. Mini review.
- Ali I, Wani WA, Saleem K. Cancer Scenario in India with Future Perspectives. *Cancer Therapy* 2011; 8: 56-70.
- Allémann E, Basseur N, Benrezzak O, Rousseau J, Kudrevich SV, Boyle RW, Leroux JC, Gurny R, Van Lier JE. PEG-coated poly(lactic acid) nanoparticles for the delivery of hexadecafluoro zinc phthalocyanine to EMT-6 mouse mammary tumours. *J Pharm Pharmacol.* 1995; 47(5):382-7. PubMed PMID: 7494187.
- Allen LC, Michalko K, Coons C. More on cephalosporin interference with creatinine determinations. *Clin Chem* 1982; 28(3):555–556.
- Anderson RF, Shinde S S, Hay MP, Gamage SA, Denny WA. Activation of 3-amino-1,2,4-benzotriazine 1,4-dioxide antitumor agents to oxidizing species following their one-electron reduction. *J Am Chem Soc.* 2003; 125: 748–756.
- Anderson T W, Yu, McGregor D B. Comet assay responses as indicators of carcinogen exposure. *Mutagenesis*, 1998; 13: 539-555.
- Anis KV, Rajeshkumar NV, Ramadasan K. Inhibition of chemical carcinogenesis by berberine in rats and mice. *J Pharm Pharmacol* 2001; 53: 763-768.
- Aries P, Paradis P, Lefevre C, Schwartz RJ, Nemer M. Essential role of GATA-4 in cell survival and drug-induced cardiotoxicity. *Proc Natl Acad Sci USA* 2004; 101: 6975–6980.
- Auyeung KK, Ko JK. *Coptis chinensis* inhibits hepatocellular carcinoma cell growth through nonsteroidal anti-inflammatory drug-activated gene activation. *Int J Mol Med.* 2009; 24(4):571–577.
- B´arcena C, Sra AK, Gao J. Applications of Magnetic Nanoparticles in Biomedicine. Liu JP et al. (eds.), *Nanoscale Magnetic Materials and Applications*, p591-626.
- Bachur NR, Gordon SL, Gee MV. NADPH cytochrome P-450 reductase activation of quinine anticancer agents to free radicals. *Proc Natl Acad Sci USA.* 1979; 76: 954–7.

- Bae YH, Park K. Targeted drug delivery to tumors: myths, reality and possibility. *J Control Release*. 2011 Aug 10;153(3):198-205. doi:10.1016/j.jconrel.2011.06.001. PubMed PMID: 21663778.
- Bai M, Shen M, Teng Y, Sun Y, Li F, Zhang X, Xu Y, Duan Y, Du L. Enhanced therapeutic effect of Adriamycin on multidrug resistant breast cancer by the ABCG2-siRNA loaded polymeric nanoparticles assisted with ultrasound. *Oncotarget*. 2015; 6(41):43779-90. doi: 10.18632/oncotarget.6085. PubMed PMID: 26575421; PubMed Central PMCID: PMC4791266.
- Bar-Sela G, Epelbaum R, Schaffer M. Curcumin as an anti-cancer agent: review of the gap between basic and clinical applications. *Curr Med Chem*. 2010; 17(3):190-7. Review. PubMed PMID: 20214562.
- Baselga J. Why the epidermal growth factor receptor? The rationale for cancer therapy. *Oncologist*. 2002; 7 Suppl 4:2-8. Review. PubMed PMID: 12202782.
- Bava A, Gornati R, Cappellini F, Caldinelli L, Pollegioni L, Bernardini G. D-amino acid oxidase-nanoparticle system: a potential novel approach for cancer enzymatic therapy. *Nanomedicine (Lond)*. 2013; 8(11):1797-806. doi: 10.2217/nnm.12.187. PubMed PMID: 23384700.
- Baylin SB, Jones PA. A decade of exploring the cancer epigenome - biological and translational implications. *Nat Rev Cancer*. 2011; 11:726-734. [PubMed: 21941284].
- Béduneau A, Saulnier P, Hindré F, Clavreul A, Leroux JC, Benoit JP. Design of targeted lipid nanocapsules by conjugation of whole antibodies and antibody Fab' fragments. *Biomaterials*. 2007; 28(33):4978-90. PubMed PMID: 17716725.
- Benlloch M, Ortega A, Ferrer P, Segarra R, Obrador E, Asensi M, Carretero J, Estrela JM. Acceleration of glutathione efflux and inhibition of gamma-glutamyltranspeptidase sensitize metastatic B16 melanoma cells to endothelium-induced cytotoxicity. *J Biol Chem*. 2005; 280(8):6950-9. PubMed PMID: 15561710.
- Berchner-Pfannschmidt U, Tug S, Kirsch M, Fandrey J. Oxygen-sensing under the influence of nitric oxide. *Cell Signal*. 2010; 22(3):349-56. doi: 10.1016/j.cellsig.2009.10.004.
- Berlin V, Haseltine WA. Reduction of Adriamycin to a semiquinone-free radical by NADPH cytochrome P-450 reductase produces DNA cleavage in a reaction mediated by molecular oxygen. *J Biol Chem*. 1981; 256: 4747-56.

- Bernier J, Hall EJ, Giaccia A. Radiation oncology: a century of achievements. *Nature*, 2004; 4:737-747.
- Bhuvanewari V, Nagini S. Lycopene: a review of its potential as an anticancer agent. *Curr Med Chem Anticancer Agents*. 2005; 5(6):627-35. Review. PubMed PMID: 16305484.
- Bible KC, Kaufmann SH. Flavopiridol: a cytotoxic flavone that induces cell death in noncycling A549 human lung carcinoma cells. *Cancer Res*. 1996; 56(21):4856-61. PubMed PMID: 8895733.
- Bindseil KU, Jakupovic J, Wolf D, Lavayre J, Leboul J, van der Pyl D. Pure compound libraries; a new perspective for natural product based drug discovery. *Drug Discov Today*. 2001; 6(16):840-847. PubMed PMID: 11495757.
- Binley K, Askham Z, Martin L, Spearman H, Day D, Kingsman S, Naylor S. Hypoxia-mediated tumour targeting. *Gene Ther*. 2003 Apr;10(7):540-9. PubMed PMID: 12646859.
- Bishayee A, Politis T, Darvesh AS. Resveratrol in the chemoprevention and treatment of hepatocellular carcinoma. *Cancer Treat Rev*. 2010; 36(1):43-53. doi: 10.1016/j.ctrv.2009.10.002. Review. PubMed PMID: 19910122.
- Bodley A, Liu LF, Israel M, Seshadri R, Koseki Y, Giuliani FC, et al. DNA Topoisomerase II-mediated interaction of Doxorubicin and Daunorubicin congeners with DNA. *Cancer Res*. 1989; 49: 5969-78.
- Bonsnes RW, Taussky HH. On the colorimetric determination of creatinine by the Jaffe reaction. *J Biol Chem*. 1945; 158: 581-591.
- Brito DA, Yang Z, Rieder CL. Microtubules do not promote mitotic slippage when the spindle assembly checkpoint cannot be satisfied. *J Cell Biol*. 2008; 182(4): 623-9. doi:10.1083/jcb.200805072.
- Brown JM, Wilson WR. Exploiting tumour hypoxia in cancer treatment. *Nat Rev Cancer*. 2004; 4(6): 437-447. Review. PubMed PMID: 15170446.
- Brown JM. Exploiting the hypoxic cancer cell: mechanisms and therapeutic strategies. *Mol Med Today* 2000; 6: 157-62.
- Brown JM. SR 4233 (tirapazamine): a new anticancer drug exploiting hypoxia in solid tumours. *Br J Cancer*. 1993; 67: 1163-1170.
- Buege JA, Aust SD. Microsomal lipid peroxidation. *Methods Enzymol*. 1978; 52:302-10. PubMed PMID: 672633.

- Burke B, Tang N, Corke KP, Tazzyman D, Ameri K, Wells M, Lewis CE. Expression of HIF-1 α by human macrophages: implications for the use of macrophages in hypoxia-regulated cancer gene therapy. *J Pathol.* 2002; 196(2): 204-12. PubMed PMID: 11793372.
- Burt HM, Zhang X, Toleikis P, Embree L, Hunter WL. Development of copolymers of poly(d, l-lactide) and methoxypolyethylene glycol as micellar carriers of paclitaxel, *Colloids Surf B Biointerfaces*, 1999; 16:161–171.
- Cai D, Mataraza JM, Qin ZH, Huang Z, Huang J, Chiles TC, Carnahan D, Kempa K, Ren Z. Highly efficient molecular delivery into mammalian cells using carbon nanotube spearing. *Nat Methods*, 2005; 2(6):449-54. PubMed PMID: 15908924.
- Candelaria M, Garcia-Arias A, Cetina L, Dueñas-Gonzalez A. Radiosensitizers in cervical cancer. Cisplatin and beyond. *Radiation Oncology (London, England)*, 2006; 1:15. doi:10.1186/1748-717X-1-15.
- Canel C, Moraes RM, Dayan FE, Ferreira D. Molecules of Interest: Podophyllotoxin. *Phytochem.*2000; 54(2):115–120. doi:10.1016/s0031-9422(00)00094-7.
- Cao W, Chi WH, Wang J, Tang JJ, Lu YJ. TNF- α promotes Doxorubicin-induced cell apoptosis and anti-cancer effect through down regulation of p21 in p53-deficient tumor cells. *Biochem Biophys Res Commun.* 2005; 330(4):1034-40. PubMed PMID: 15823547.
- Cao W, Mab SL, Tanga J, Shic J, Lu Y. A combined treatment TNF- α /Doxorubicin alleviates the resistance of MCF-7/Adr cells to cytotoxic treatment. *Biochim Biophys Acta – Mol Cell Res.*2006; 1763(2):182–187. doi:10.1016/j.bbamcr.2005.12.008.
- Carmeliet P, Jain RK. Angiogenesis in cancer and other diseases. *Nature.* 2000; 407:49 – 57.
- Carretero J, Obrador E, Anasagasti MJ, Martin JJ, Vidal-Vanaclocha F, Estrela JM. Growth-associated changes in glutathione content correlate with liver metastatic activity of B16 melanoma cells. *Clin Exp Metastasis.* 1999; 17(7):567-74. PubMed PMID: 10845555.
- Carvalho C, Santos RX, Cardoso S, Correia S, Oliveira PJ, Santos MS, Moreira PI. Doxorubicin: the good, the bad and the ugly effect. *Curr Med Chem.* 2009; 16(25):3267-85. Epub 2009 Sep 1. Review. PubMed PMID: 19548866.

- Cerda H, Delincée H, Haine H, Rupp H. The DNA 'comet assay' as a rapid screening technique to control irradiated food. *Mutat Res.* 1997, 29; 375(2):167-81. PubMed PMID: 9202727.
- Cerdan S, Lötscher HR, Künnecke B, Seelig J. Monoclonal antibody-coated magnetite particles as contrast agents in magnetic resonance imaging of tumors. *Magn Reson Med.* 1989; 12(2):151-63. PubMed PMID: 2615625.
- Chaffer CL, Weinberg RA. A perspective on cancer cell metastasis. *Science*, 2011; 331:1559-1564.
- Chang KS. Down-regulation of c-Ki-ras2 gene expression associated with morphologic differentiation in human embryonal carcinoma cells treated with berberine. *J Formos Med Assoc.* 1991; 90:10–14.
- Chatterjee K, Zhang J, Honbo N, Karliner JS. Doxorubicin Cardiomyopathy. *Cardiology*, 2010; 115(2):155-162. doi:10.1159/000265166
- Chen GG, Lai PB, Hu X, Lam IK, Chak EC, Chun YS, Lau WY. Negative correlation between the ratio of Bax to Bcl-2 and the size of tumor treated by culture supernatants from Kupffer cells. *Clin Exp Metastasis*, 2002; 19(5):457-64. PubMed PMID: 12198774.
- Chen J, Keltner L, Christophersen J, Zheng F, Krouse M, Singhal A, Wang SS. New technology for deep light distribution in tissue for phototherapy. *Cancer J.* 2002; 8(2):154-63. PubMed PMID: 11999949.
- Chidambara Murthy KN, Jayaprakasha GK, Patil BS. The natural alkaloid berberine targets multiple pathways to induce cell death in cultured human colon cancer cells. *Eur J Pharmacol.* 2012; 688(1-3):14-21. doi:10.1016/j.ejphar.2012.05.004. PubMed PMID: 22617025.
- Choi MS, Yuk DY, Oh JH, Jung HY, Han SB, Moon DC, Hong JT. Berberine inhibits human neuroblastoma cell growth through induction of p53-dependent apoptosis. *Anticancer Res.* 2008; 28(6A):3777-84. PubMed PMID: 19189664.
- Chomczynski P, Sacchi N. Single step method of RNA isolation by acid guanidium thiocyanate- phenol- chloroform extraction. *Anal Biochem* 1987; 162: 156- 159.
- Chomczynski P, Sacchi N. Single step method of RNA isolation by acid guanidium thiocyanate- phenol- chloroform extraction. *Anal Biochem.* 1987; 162: 156- 59.

- Chomczynski P, Sacchi N. The single-step method of RNA isolation by acid guanidinium thiocyanate-phenol-chloroform extraction: twenty-something years on. *Nat Protoc.* 2006; 1(2):581-5. PubMed PMID: 17406285.
- Coleman CN, Bump EA, Kramer RA. Chemical modifiers of cancer treatment. *J Clin Oncol.* 1988; 6(4):709-33. Review. PubMed PMID: 3282035.
- Corot C, Robert P, Idee JM, Port M. Recent advances in iron oxide nanocrystal technology for medical imaging. *Adv Drug Deliv Rev.* 2006; 58:1471–1504.
- Correia AL, Bissell MJ. The tumor microenvironment is a dominant force in multidrug resistance. *Drug Resist Updat.* 2012;15(1-2):39-49. doi:10.1016/j.drug.2012.01.006. Review. PubMed PMID: 22335920.
- Cosse JP, Michiels C. Tumour hypoxia affects the responsiveness of cancer cells to chemotherapy and promotes cancer progression. *Anticancer Agents Med Chem.* 2008; 8(7):790-7. Review. PubMed PMID: 18855580.
- Craig WJ. Health-promoting properties of common herbs. *Am J Clin Nutr.* 1999; 70:S491–9.
- Culling CA. Hand book of histopathological and histochemical techniques: including museum techniques. 3rd ed. London: Butterworth. 1974.
- Cummings J, Anderson L, Willmott N, Smyth JF. The molecular pharmacology of doxorubicin *in vivo*. *Eur J Cancer,* 1991; 27: 532–35.
- Cutts JH, Beer CT, Noble AL. Biological Properties of Vincalukoblastine, an Alkaloid in *Vinca rosea* Linn, with Reference to Its Antitumor Action. *Cancer Res.,* 1960; 20:1023-1031.
- Damia G, D'Incalci M. Mechanisms of resistance to alkylating agents. *Cytotechnology,*1998; 27(1-3):165–73. doi:10.1023/A:1008060720608. PMID: 19002790.
- Daniels JS, Gates KS. DNA cleavage by the antitumor agent 3-amino-1,2,4-benzotriazine 1,4-dioxide (SR4233): Evidence for involvement of hydroxyl radical. *J Am Chem Soc.*1996; 118: 3380–3385.
- Daniels-Wells TR, Penichet ML. Transferrin receptor 1: a target for antibody-mediated cancer therapy. *Immunotherapy.* 2016. [Epub ahead of print] PubMed PMID: 27373880.
- Das T, Chakraborty S, Banerjee S, Mukherjee A, Samuel G, Sarma HD, Nair CK, Kagiya VT, Venkatesh M. Preparation and preliminary biological evaluation of a 177Lu

- labeled sanazole derivative for possible use in targeting tumor hypoxia. *Bioorg Med Chem.* 2004; 12(23):6077-84. PubMed PMID: 15519153.
- De Ridder M, Van Esch G, Engels B, Verovski V, Storme G. Hypoxic tumor cell radiosensitization: role of the iNOS/NO pathway. *Bull Cancer*, 2008; 95(3):282-91. doi: 10.1684/bdc.2008.0592.
- Delaney G, Jacob S, Featherstone C, Barton M. The role of radiotherapy in cancer treatment: estimating optimal utilization from a review of evidence-based clinical guidelines. *Cancer*, 2005; 104:1129-1137.
- Denko NC. Hypoxia, HIF1 and glucose metabolism in the solid tumour. *Nat Rev Cancer.* 2008; 8(9):705-13. doi: 10.1038/nrc2468.
- Denny WA, Wilson WR. Bioreducible mustards: a paradigm for hypoxia-selective prodrugs of diffusible cytotoxins (HPDCs). *Cancer and Metastasis Reviews.* 1993; 12: 135-151.
- Desser RK, Himmelhoch SR, Evans WH, Januska M, Mage M, Shelton E. Guinea pig heterophil and eosinophil peroxidase. *Arch Biochem Biophys.* 1972; 148(2):452-65. PubMed PMID: 4623114.
- Divakaran SA, Sreekanth KM, Rao KV, Nair CKK. D-aminoacid oxidase-Fe₂O₃ nanoparticle complex mediated antitumor activity in *Swiss albino* mice. *J Cancer Ther.* 2011; 2:666-674. doi:10.4236/jct.2011.25089.
- Dobrowsky W, Huigol NG, Jayatilake RS, Kizilbash NI, Okkan S, Kagiya TV, et al. AK-2123 (Sanazole) as a radiation sensitizer in the treatment of stage II cancer cervix; initial results of an IAEA multicentre randomized trial. *J Cancer Res.* 2005; 1:75-8.
- Dorie MJ, Brown JM. Tumor-specific, schedule dependent interaction between tirapazamine (SR 4233) and cisplatin. *Cancer Res.* 1993; 53:4633-4636.
- Doroshov JH, Locker GY, Baldinger J, Myers CE. The effect of doxorubicin on hepatic and cardiac glutathione. *Res Commun Chem Pathol Pharmacol.* 1979; 26:285-295.
- Doroshov JH. Effect of anthracycline antibiotics on oxygen radical formation in rat heart. *Cancer Res.* 1983; 43:460-472.
- Dorr RT. Bleomycin pharmacology: mechanism of action and resistance, and clinical pharmacokinetics. *Semin Oncol.* 1992; 19(Suppl 5): 3-8. PMID: 1384141.
- Doumas B T, Ard Watson W, Biggs H G. Albumin standards and the measurement of serum albumin with bromocresol green. *Clin Chim Acta*, 1971; 31(1):87-96.

- Duvillard C, Romanet P, Cosmidis A, Beaudouin N, Chauffert B. Phase 2 study of intratumoral cisplatin and epinephrine treatment for locally recurrent head and neck tumors. *Ann Otol Rhinol Laryngol.*2004; 113(3 Pt 1):229-33. PubMed PMID: 15053208.
- Ellerby HM, Bredesen DE, Fujimura S, John V. Hunter-killer peptide (HKP) for targeted therapy. *J Med Chem.* 2008; 51(19):5887-92. doi:10.1021/jm800495u. PubMed PMID: 18828573.
- Farinati F, Cardin R, Cassaro M, Bortolami M, Nitti D, Tieppo C, et al. Helicobacter pylori, inflammation, oxidative damage and gastric cancer: a morphological, biological and molecular pathway. *Eur J Cancer Prev.* 2008; 17:195–200.
- Fernández-Pacheco R, Valdivia JG, Ibarra MR. Magnetic nanoparticles for local drug delivery using magnetic implants. *Methods Mol Biol.* 2009; 544:559-69. doi:10.1007/978-1-59745-483-4_35. PubMed PMID: 19488723.
- Ferreira AC, Isomoto H, Moriyama M, Fujioka T, Machado JC, Yamaoka Y. Helicobacter and gastric malignancies. *Helicobacter* 2008; 13 (Suppl 1): 28–34.
- Firn RD, Jones CG. Natural products - a simple model to explain chemical diversity. *Nat Prod Rep.* 2003; 20:382–391.10.1039/b208815k. PubMed: 12964834.
- Flamant L, Notte A, Ninane N, Raes M, Michiels C. Anti-apoptotic role of HIF-1 and AP-1 in paclitaxel exposed breast cancer cells under hypoxia. *Mol Cancer.* 2010; 9:191. doi: 10.1186/1476-4598-9-191. PubMed PMID: 20626868.
- Folkman J, Long DM. The use of silicone rubber as a carrier for prolonged drug therapy. *Surg Res.* 1964; 4:139–142.
- Fornari FA, Randolph JK, Yalowich JC, Ritke MK, Gewirtz DA. Interference by doxorubicin with DNA unwinding in MCF-7 breast tumor cells. *Mol Pharmacol.* 1994; 45: 649–56.
- Forssen EA, Malé-Brune R, Adler-Moore JP, Lee MJ, Schmidt PG, Krasieva TB, Shimizu S, Tromberg BJ. Fluorescence imaging studies for the disposition of daunorubicin liposomes (DaunoXome) within tumor tissue. *Cancer Res.* 1996; 56(9):2066-75. PubMed PMID: 8616852.
- Fox ME, Lemmon MJ, Mauchline ML, Davis TO, Giaccia AJ, Minton NP, Brown JM. Anaerobic bacteria as a delivery system for cancer gene therapy: in vitro activation of 5-fluorocytosine by genetically engineered clostridia. *Gene Ther.* 1996; 3(2): 173-8. Erratum in: *Gene Ther* 1996; 3(8): 741. PubMed PMID: 8867865.

- Franovic A, Gunaratnam L, Smith K, et al. Translational up-regulation of the EGFR by tumor hypoxia provides a non-mutational explanation for its overexpression in human cancer. *Proc Natl Acad Sci U S A*, 2007;104:13092-13097.
- Franzblau SG, Cross C. Comparative in vitro antimicrobial activity of Chinese medicinal herbs. *J Ethnopharmacol*.1986; 15:279–288.
- Fukuda K, Hibiya Y, Mutoh M, Koshiji M, Akao S, Fujiwara H. Inhibition of activator protein 1 activity by berberine in human hepatoma cells. *Planta Med*.1999; 65(4):381-3. PubMed PMID: 10364850.
- García-Angulo AH, Kagiya VT. Intratumoral and parametrial infusion of a 3-nitrotriazole (AK-2123) in the radiotherapy of the uterine cervix cancer: stage II-III--preliminary positive results. *Int J Radiat Oncol Biol Phys*. 1992; 22(3):589-91. PubMed PMID: 1735697.
- Gardlik R, Behuliak M, Palffy R, Celec P, Li CJ. Gene therapy for cancer: bacteria-mediated anti-angiogenesis therapy. *Gene Ther*. 2011; 18(5): 425-431. doi: 10.1038/gt.2010.176. Epub 2011 Jan 13. Review. PubMed PMID: 21228886.
- Gelderman KA, Tomlinson S, Ross GD, Gorter A. Complement function in mAb-mediated cancer immunotherapy. *Trends Immunol*.2004; 25(3):158–64. doi:10.1016/j.it.2004.01.008. PMID 15036044.
- Gerhardt W, Waldenström J. Creatine kinase B-subunit activity in serum after immune inhibition of M-subunit activity. *Clin Chem*.1979; 25:1274-1280.
- Gerweck LE, Vijayappa S, Kozin S. Tumor pH controls the in vivo efficacy of weak acid and base chemotherapeutics. *Mol Cancer Ther*. 2006; 5:1275-9.
- Ghattass K, Assah R, El-Sabban M, Gali-Muhtasib H. Targeting hypoxia for sensitization of tumors to radio- and chemotherapy. *Curr Cancer Drug Targets*,2013; 13(6):670–685.
- Gilkes DM, Semenza GL. Role of hypoxia-inducible factors in breast cancer metastasis. *Future Oncol*.2013; 9(11):1623-36.
- Glöckl G, Hergt R, Zeisberger M, Dutz S, Nagel S, Weitschies W. The effect of field parameters, nanoparticle properties and immobilization on the specific heating power in magnetic particle hyperthermia. *J Phys: Condens Matter*, 2006; 18:S2935–S2949.
- Goldberg MA, Dunning SP, Bunn HF. Regulation of the erythropoietin gene: evidence that the oxygen sensor is a heme protein. *Science*. 1988; 242(4884):1412-5.

- Goncharova SA, Raevskaia TA, Konovalova NP, Kagiia VT. The radiosensitizer AK-2123 enhances sensitivity of MDR-tumors to Mitomycin C. *Vopr Onkol.* 2000; 46(2):202-8. Russian. PubMed PMID: 10853422.
- Goodwin SC, Bittner CA, Peterson CL, Wong G. Single-dose toxicity study of hepatic intra-arterial infusion of doxorubicin coupled to a novel magnetically targeted drug carrier. *Toxicol Sci* 2001; 60: 177-83.
- Gornall AG, Bardawill CJ, David MM. Determination of serum proteins by means of the biuret reaction. *J Biol Chem.* 1949; 177(2):751-66. PubMed PMID:18110453.
- Gradishar WJ, Tjulandin S, Davidson N, Shaw H, Desai N, Bhar P, et al. Phase III trial of nanoparticle albumin-bound paclitaxel compared with polyethylated castor oil-based paclitaxel in women with breast cancer. *J Clin Oncol.* 2005; 23: 7794-803.
- Gray LH, Conger AD, Eben M, Hornsey S and Scott OC. Concentration of oxygen dissolved in tissues at the time of irradiation as a factor in radiotherapy. *Br J Radiol* 1953; 26: 638-648.
- Greco F, Vicent MJ. Combination therapy: opportunities and challenges for polymer-drug conjugates as anticancer nanomedicines. *Adv Drug Deliv Rev.* 2009; 61(13):1203-13. doi: 10.1016/j.addr.2009.05.006.
- Greco O, Dachs GU. Gene directed enzyme/pro-drug therapy of cancer: historical appraisal and future prospectives. *J Cell Physiol.* 2001; 187:22–36.
- Greish K. Enhanced permeability and retention of macromolecular drugs in solid tumors: a royal gate for targeted anticancer nanomedicines. *J Drug Target.*2007; 15(7-8):457-64. Review. PubMed PMID: 17671892.
- Griffiths L, Binley K, Iqball S, Kan O, Maxwell P, Ratcliffe P, Lewis C, Harris A, Kingsman S, Naylor S. The macrophage - a novel system to deliver gene therapy to pathological hypoxia. *Gene Ther.*2000; 7(3):255-62. PubMed PMID: 10694803.
- Grisendi S, Mecucci C, Falini B, Pandolfi PP. Nucleophosmin and cancer. *Nat Rev Cancer.*2006; 6:493-505. Doi: 10.1038/nrc1885.
- Grisham MB, Johnson GG, Lancaster JR Jr. Quantitation of nitrate and nitrite in extracellular fluids. *Methods Enzymol.*1996; 268:237-46. PubMed PMID: 8782590.
- Guéritte-Voegelein F, Guénard D, Potier P. Anticancer substances of vegetable origin. Spindle poisons: vincalukoblastine, leurocristine and navelbine; taxol and taxotere. *C R Seances Soc Biol Fil.* 1992; 186(5):433-40. French. PubMed PMID: 1363958.

- Guo YS, Jin GF, Houston CW, Thompson JC, Townsend CM Jr. Insulin-like growth factor-I promotes multidrug resistance in MCLM colon cancer cells. *J Cell Physiol* 1998; 175: 141- 8.
- Gupta AK, Gupta M. Synthesis and surface engineering of iron oxide nanoparticles for biomedical applications. *Biomaterials*,2005; 26(18):3995-4021. Review. PubMed PMID: 15626447.
- Gupta J, Bhargava P, Bahadur D. Methotrexate conjugated magnetic nanoparticle for targeted drug delivery and thermal therapy. *J Appl Phys.* 014; 115: 17B516.
- Hafeman DG, Sunde RA, Hoekstra WG. Effect of dietary selenium on erythrocyte and liver glutathione peroxidase in the rat. *J Nutr.*1974; 104(5):580-7. PubMed PMID: 4823943.
- Hall EJ, Roizin-Towle L. Hypoxic sensitizers: Radiobiological studies at the cellular level. *Radiology* 117: 453-457, 1975.
- Hamm CA, Stevens JW, Xie H, Vanin EF, Morcuende JA, Abdulkawy H, Seftor EA, Sredni ST, Bischof JM, Wang D, Malchenko S, Bonaldo Mde F, Casavant TL, Hendrix MJ, Soares MB. Microenvironment alters epigenetic and gene expression profiles in Swarm rat chondrosarcoma tumors. *BMC Cancer*, 2010; 10:471. doi:10.1186/1471-2407-10-471.
- Hanahan D, Weinberg R. Hallmarks of Cancer: The Next Generation. *Cell*, 2011; 144:646–674.
- Harikumar KB, Kuttan G, Kuttan R. Inhibition of progression of erythroleukemia induced by Friend virus in Balb/C mice by natural products-berberine, curcumin and picroliv. *J Exp Ther Oncol.*2008; 7:275–284.
- Hashizume H, Baluk P, Morikawa S, McLean JW, Thurston G, Roberge S, Jain RK, McDonald DM. Openings between defective endothelial cells explain tumor vessel leakiness. *Am J Pathol.* 2000 Apr;156(4):1363-80. PubMed PMID: 10751361; PubMed Central PMCID: PMC1876882.
- Henry RJ, Cannon DC, Winkelman JW. *Clinical Chemistry: Principles and Technics*, 2nd ed. New York: Harper and Row; 1974:522-525.
- Henry RJ. Determination of total protein by colorimetric method. In: *Clinical Chemistry*, p. 181, Harper and Row Publ., New York: NY, USA; 1964:181.

- Hergt R, Dutz S, Müller R and Zeisberger M. Magnetic particle hyperthermia: nanoparticle magnetism and materials development for cancer therapy. *J Phys:Condens Matter*, 2006; 18:S2919–S2934.
- Hirn S, Semmler-Behnke M, Schleh C, Wenk A, Lipka J, Schäffler M, Takenaka S, Möller W, Schmid G, Simon U, et al. Particle size-dependent and surface charge-dependent biodistribution of gold nanoparticles after intravenous administration. *Eur J Pharm Biopharm*. 2011; 77:407–416.
- Ho YT, Lu CC, Yang JS, Chiang JH, Li TC, Ip SW, Hsia TC, Liao CL, Lin JG, Wood WG, Chung JG. Berberine induced apoptosis via promoting the expression of caspase-8, -9 and -3, apoptosis-inducing factor and endonuclease G in SCC-4 human tongue squamous carcinoma cancer cells. *Anticancer Res*. 2009; 29(10):4063-70. PubMed PMID: 19846952.
- Ho YT, Yang JS, Lu CC, Chiang JH, Li TC, Lin JJ, et al. Berberine inhibits human tongue squamous carcinoma cancer tumor growth in a murine xenograft model. *Phytomedicine* 2009; 16:887–890.
- Hoffman AS. The origins and evolution of “controlled” drug delivery systems. *J Control Release*, 2008; 132:153–163.
- Hsu WH, Hsieh YS, Kuo HC, Teng CY, Huang HI, Wang CJ, Yang SF, Liou YS, Kuo WH. Berberine induces apoptosis in SW620 human colonic carcinoma cells through generation of reactive oxygen species and activation of JNK/p38 MAPK and FasL. *Arch Toxicol*. 2007; 81(10):719-28. PubMed PMID: 17673978.
- Hu CM, Aryal S, Zhang L. Nanoparticle-assisted combination therapies for effective cancer treatment. *Ther Deliv*. 2010; 1(2):323-34. Review. PubMed PMID: 22816135.
- Huan LC, Hua BY. Clinical pharmacokinetic study and sensitive effect of AK-2123. *Int J Radiat Oncol Biol Phys*. 1994; 29(3):607-10. PubMed PMID: 8005824.
- Huang C, Tang Z, Zhou Y, Zhou X, Jin Y, Li D, Yang Y, Zhou S. Magnetic micelles as a potential platform for dual targeted drug delivery in cancer therapy. *Int J Pharm*, 2012; 429:113-22.
- Huilgol NG, Chatterjee N, Mehta AR. An overview of the initial experience with AK-2123 as a hypoxic cell sensitizer with radiation in the treatment of advanced head and neck cancers. *Int J Radiat Oncol Biol Phys*. 1996; 34(5):1121-4. PubMed PMID: 8600096.
- Huilgol NG, Nair CKK, Kagia VT (Eds). *Radio sensitizers- a contemporary audit*. 2000, Narosa publishing house, New Delhi, India.

- Huth S, Lausier J, Gersting SW, Rudolph C, Plank C, Welsch U, Rosenecker J. Insights into the mechanism of magnetofection using PEI-based magnetofectins for gene transfer. *J Gene Med.* 2004; 6(8):923-36. PubMed PMID: 15293351.
- Iizuka N, Miyamoto K, Okita K, Tangoku A, Hayashi H, Yosino S, Abe T, Morioka T, Hazama S, Oka M. Inhibitory effect of Coptidis Rhizoma and berberine on the proliferation of human esophageal cancer cell lines. *Cancer Let.* 2000; 148:19–25.
- Imamura M, Edgren M, Murata T, Nagata K, Isoda H, Akagi K, Revesz L, Tanaka Y. Radiosensitization with a 3-nitrotriazole (ak-2123). *Int J Oncol.* 1995; 6(4):841-5. PubMed PMID: 21556609.
- Imamura M, Edgren M, Murata T, Nagata K, Isoda H, Akagi K, Revesz L, Tanaka Y. Radiosensitization with a 3-nitrotriazole (ak-2123). *Int J Oncol.* 1995; 6(4):841-5. PubMed PMID: 21556609.
- Imanshahidi M, Hosseinzadeh H. Pharmacological and therapeutic effects of *Berberis vulgaris* and its active constituent, berberine. *Phytother Res.* 2008; 22:999–1012.
- Jackson SP, Bartek J. The DNA-damage response in human biology and disease. *Nature* 2009; 461:1071-1078.
- Jain A, Jain SK. PEGylation: an approach for drug delivery. A review. *Crit Rev Ther Drug Carrier Syst.* 2008; 25(5):403-47. Review. PubMed PMID: 19062633.
- Jain KK. Use of bacteria as anticancer agents. *Expert Opin Biol Ther.* 2001; 1(2):291-300. Review. PubMed PMID: 11727536.
- Jain RK. Tumor angiogenesis and accessibility: role of vascular endothelial growth factor. *Semin Oncol.* 2002; 29:3-9.
- James MA, Fu H, Liu Y, Chen DR, You M. Dietary administration of berberine or Phellodendron amurense extract inhibits cell cycle progression and lung tumorigenesis. *Mol Carcinog.* 2011; 50(1):1-7. doi: 10.1002/mc.20690. PubMed PMID: 21061266.
- Janero DR. Malondialdehyde and thiobarbituric acid-reactivity as diagnostic indices of lipid peroxidation and peroxidative tissue injury. *Free Radic Biol Med.* 1990; 9(6):515-40. Review. PubMed PMID: 2079232.
- Jantova S, Cipak L, Cernakova M, Kostalova D. Effect of berberine on proliferation, cell cycle and apoptosis in HeLa and L1210 cells. *J Pharm Pharmacol.* 2003; 55:1143–9.
- Jarvelainen H, Sainio A, Koulu M, Wight TN, Penttinen R. Extracellular matrix molecules: potential targets in pharmacotherapy. *Pharmacol. Rev.* 2009; 61: 198-223.

- Jayakumar OD, Ganguly R, Tyagi AK, Chandrasekharan DK, Nair CK. Water dispersible Fe₃O₄ nanoparticles carrying doxorubicin for cancer therapy. *J Nanosci Nanotechnol.* 2009; 9(11):6344-8. PubMed PMID: 19908532.
- Jayakumar OD, Ganguly R, Tyagi AK, Chandrasekharan DK, Nair CK. Water dispersible Fe₃O₄ nanoparticles carrying doxorubicin for cancer therapy. *J Nanosci Nanotechnol.* 2009; 9(11):6344-8. PubMed PMID: 19908532.
- Ji JL, Huang XF, Zhu HL. Curcumin and its formulations: potential anti-cancer agents. *Anticancer Agents Med Chem.* 2012; 12(3):210-8. Review. PubMed PMID: 22044005.
- Jiang W, Kim BYS, Rutka JT, Chan WCW. Nanoparticle-mediated cellular response is size-dependent. *Nat Nanotechnol.* 2008; 3:145–150.
- Jin H, Heller DA, Sharma R, Strano MS. Size-dependent cellular uptake and expulsion of single-walled carbon nanotubes: single particle tracking and a generic uptake model for nanoparticles. *ACS Nano.* 2009; 3:149–158.
- Jing Y, Ma N, Fan T, Wang C, Bu X, Jiang G, Li R, Gao L, Li D, Wu M, Wei L. Tumor necrosis factor-alpha promotes tumor growth by inducing vascular endothelial growth factor. *Cancer Invest.* 2011; 29(7):485-93. doi:10.3109/07357907.2011.597812. PubMed PMID: 21740086.
- John C. Interpretation of Infrared Spectra, a Practical Approach. In: Meyers R A, editors. *Encyclopedia of Analytical Chemistry*, Newtown, USA: John Wiley & Sons Ltd, Chichester 2000: 10815–10837.
- Johnson IS, Wright HF, Svoboda GH, Vlantis J. Antitumor Principles Derived from *Vinca rosea* Linn. *Cancer Res.*, 1960; 20:1016-1022.
- Jordan A, Hadfield JA, Lawrence NJ, McGown AT. Tubulin as a target for anticancer drugs: agents which interact with the mitotic spindle. *Med Res Rev.* 1998; 18(4):259-96. Review. PubMed PMID: 9664292.
- Jung HY, Fattet L, Yang J. Molecular pathways: linking tumor microenvironment to epithelial-mesenchymal transition in metastasis. *Clin Cancer Res* 2015; 21: 962–8.
- Kaneshiro TL, Lu ZR. Targeted intracellular co-delivery of chemotherapeutics and nucleic acid with a well-defined dendrimer-based nanoglobular carrier. *Biomaterials*, 2009; 30(29):5660–5666.
- Kang MR, Chung IK. Down-regulation of DNA topoisomerase II alpha in human colorectal carcinoma cells resistant to a protoberberine alkaloid, berberrubine. *Mol Pharmacol* 2002; 61:879–884.

- Kang S, Li Z, Yin Z, Jia R, Song X, Li L, Chen Z, Peng L, Qu J, Hu Z, Lai X, Wang G, Liang X, He C, Yin L. The antibacterial mechanism of berberine against *Actinobacillus pleuropneumoniae*. *Nat Prod Res*. 2015; 29(23):2203-6. doi:10.1080/14786419.2014.1001388.
- Karpagam P, Nair CKK, Tsutomu VK. Effect of a hypoxic radiosensitizer, AK 2123 (Sanazole), on Yeast *Saccharomyces cerevisiae*. *J Radiat Res* 2001; 42:217–227.
- Kasai S, Nagasawa H, Yamashita M, Masui M, Kuwasaka H, Oshodani T, Uto Y, Inomata T, Oka S, Inayama S, Hori H. New antimetastatic hypoxic cell radiosensitizers: design, synthesis, and biological activities of 2-nitroimidazole- acetamide, TX-1877, and its analogues. *Bioorg Med Chem* 2001; 9: 453–64.
- Kasinski AL, Slack FJ. MicroRNAs en route to the clinic: progress in validating and targeting microRNAs for cancer therapy. *Nat Rev Cancer*. 2011; 11:849–864.
- Kassirer JP. Clinical evaluation of kidney function--glomerular function. *N Engl J Med* 1971; 285(7):385-389.
- Kasuno K, Takabuchi S, Fukuda K, Kizaka-Kondoh S, Yodoi J, Adachi T, Semenza GL, Hirota K. Nitric oxide induces hypoxia-inducible factor 1 activation that is dependent on MAPK and phosphatidylinositol 3-kinase signaling. *J Biol Chem*. 2004; 279(4):2550-8.
- Kawai Y, Anno K. Mucopolysaccharide-degrading enzymes from the liver of the squid, *Ommastrephes sloani pacificus*. I. Hyaluronidase. *Biochim Biophys Acta*.1971;242(2):428-36. PubMed PMID: 4258518.
- Kettmann V, Kostalova D, Jantova S, Cernakova M, Drimal J. In vitro cytotoxicity of berberine against HeLa and L1210 cancer cell lines. *Pharmazie* 2004; 59: 548–551.
- Khaled G. Enhanced permeability and retention of macromolecular drugs in solid tumors: A royal gate for targeted anticancer nanomedicines. *J Drug Target*, 2007; 15(7–8): 457–464.
- Kim S, Kim Y, Kim JE, Cho KH, Chung JH. Berberine inhibits TPA-induced MMP-9 and IL-6 expression in normal human keratinocytes. *Phytomedicine* 2008; 15:340–347.
- Kim Y, Ma A, Kitta K, Fitch SN, Ikeda T, Ihara Y, Simon AR, Evans T, Suzuki YJ. Anthracycline-induced suppression of GATA-4 transcription factor: implication in the regulation of cardiac myocyte apoptosis. *Mol Pharmacol*. 2003; 63: 368–377.
- Klaude M, Eriksson S, Nygren J, Ahnström G. The Comet assay: mechanism and technical considerations. *Mutat. Res*, 1996; 363: 89-96.

- Koda J, Venook A, Walser E. A multicenter, phase I/II trial of hepatic intra-arterial delivery of doxorubicin hydrochloride adsorbed to magnetic targeted carriers in patients with hepatocellular carcinoma. *Eur J Cancer* 2002; 38: S18.
- Koizumi M, Nishimura T, Kagiya T. Trial of Adverse effect inhibition with glucosides of vitamin C and vitamin E in radiotherapy and chemotherapy. *J Cancer Res Ther.* 2005; 1:39.
- Końca K, Lankoff A, Banasik A, Lisowska H, Kuszewski T, Gózdź S, Koza Z, Wojcik A. A cross-platform public domain PC image-analysis program for the comet assay. *Mutat Res.* 2003; 534(1-2):15-20. PubMed PMID: 12504751.
- Kondakova IV, Tcheredova VV, Zagrebelnaya GV, Cherdyntseva NV, Kagiya VT, andChoinzonov EL. Production of nitric oxide by hypoxic radiosensitizersanazole. *Exp Oncol.* 2004; 26(4):329-33. PubMed PMID: 15627070.
- Konerding MA, Fait E, Gaumann A. 3D microvascular architecture of precancerous lesions and invasive carcinomas of the colon. *Br J Cancer* 2001; 84:1354–62.
- Konovalova NP, Diatchkovskaya RF, Volkova LM, Kagiya TV. Radiosensitizer AK-2123 as modulating agent in the chemotherapy of experimental metastases. *Neoplasma*, 1995; 42(3):119-22. PubMed PMID: 7637820.
- Konovalova NP, Volkova LM, Tatyanyenko LV, Kotelnikova RA, Yakushchenko TN, Kagiya TV. Inhibitory effect of radiosensitizer AK-2123 on experimental hepatic metastases and Ca²⁺ active transport. *Neoplasma.* 1997; 44(6):361-5. PubMed PMID: 9605008.
- Kotamballi N. Chidambara Murthy 1, Guddadarangavvanahally K. Jayaprakasha, Bhimanagouda S. Patil The natural alkaloid berberine targets multiple pathways to induce cell death in cultured human colon cancer cells. *Eur J Pharmacol* 2012; 688: 14–21.
- Kovacs MS, Hocking DJ, Evans JW, Siim BG, Wouters BG, Brown JM. Cisplatin anti-tumour potentiation by tirapazamine results from a hypoxia-dependent cellular sensitization to cisplatin. *Br J Cancer*, 1999; 80(8):1245-51. PubMed PMID: 10376978; PubMed Central PMCID: PMC2362366.
- Krey AK, Hahn FE. Berberine: complex with DNA. *Science.* 1969; 166(3906):755-7. PubMed PMID: 5823315.

- Krötz F, de Wit C, Sohn HY, Zahler S, Gloe T, Pohl U, Plank C. Magnetofection--a highly efficient tool for antisense oligonucleotide delivery *in vitro* and *in vivo*. *Mol Ther*. 2003; 7(5 Pt 1):700-10. PubMed PMID: 12718913.
- Kung AL, Wang S, Klco JM, Kaelin WG, Livingston DM. Suppression of tumor growth through disruption of hypoxia-inducible transcription. *Nature Med*. 2000; 6: 1335–1340.
- Kuo CL, Chi CW, Liu TY. The anti-inflammatory potential of berberine *in vitro* and *in vivo*. *Cancer Lett*. 2004 20; 203(2):127-37.
- Lammers T, Peschke P, Kühnlein R, Subr V, Ulbrich K, Huber P, Hennink W, Stormy G. Effect of Intratumoral Injection on the Biodistribution and the Therapeutic Potential of HPMA Copolymer-Based Drug Delivery Systems. *Neoplasia* (New York, NY). 2006; 8(10):788-795. doi: 10.1593/neo.06436.
- Landesman-Milo D, Ramishetti S, Peer D. Nanomedicine as an emerging platform for metastatic lung cancer therapy. *Cancer Metastasis Rev*. 2015; 34(2):291-301. doi: 10.1007/s10555-015-9554-4. PubMed PMID: 25948376.
- Lazarovits J, Chen YY, Sykes EA, Chan WC. Nanoparticle-blood interactions: the implications on solid tumour targeting. *Chem Commun (Camb)*. 2015; 51(14):2756-67. doi: 10.1039/c4cc07644c. PubMed PMID: 26829150.
- Ledoux S, Yang R, Friedlander G, Laouari D. Glucose depletion enhances P-glycoprotein expression in hepatoma cells: role of endoplasmic reticulum stress response. *Cancer Res* 2003; 63: 7284- 90.
- Lee AE, Wilson WR. Hypoxia-dependent retinal toxicity of bioreductive anticancer prodrugs in mice. *Toxicol Appl Pharmacol*. 2000; 163:50–59.
- Lee S, Lim HJ, Park HY, Lee KS, Park JH, Jang Y. Berberine inhibits rat vascular smooth muscle cell proliferation and migration *in vitro* and improves neointima formation after balloon injury *in vivo*. Berberine improves neointima formation in a rat model. *Atherosclerosis*, 2006; 186:29–37.
- Lehár J, Krueger AS, Avery W, Heilbut AM, Johansen LM, Price ER, Rickles RJ, Short GF 3rd, Staunton JE, Jin X, Lee MS, Zimmermann GR, Borisy AA. Synergistic drug combinations tend to improve therapeutically relevant selectivity. *Nat Biotechnol*. 2009; 27(7):659-66. doi: 10.1038/nbt.1549. Epub 2009 Jul 5. Erratum in: *Nat Biotechnol*. 2009; 27(9):864. PubMed PMID: 19581876; PubMed Central PMCID: PMC2708317.

- Lemmon MJ, van Zijl P, Fox ME, Mauchline ML, Giaccia AJ, Minton NP, Brown JM. Anaerobic bacteria as a gene delivery system that is controlled by the tumour microenvironment. *Gene Ther.* 1997 Aug;4(8):791-6. PubMed PMID: 9338007.
- Letasiová S, Jantová S, Cipák L, Múcková M. Berberine – antiproliferative activity *in vitro* and induction of apoptosis/necrosis of the U937 and B16 cells. *Cancer Lett.* 2006; 239(2):254-62. PubMed PMID: 16229943.
- Letasiova S, Jantova S, Muckova M, Theiszova M. Antiproliferative activity of berberine *in vitro* and *in vivo*. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub.* 2005; 149:461–463.
- Leu A, Berk D, Lymboussaki A, et al. Absence of functional lymphatics within a murine sarcoma: a molecular and functional evaluation. *Cancer Res* 2000;60:4324–7.
- Levental KR, Yu H, Kass L, Lakins JN, Egeblad M, Erler JT, Fong SF, Csiszar K, Giaccia A, Weninger W, Yamauchi M, Gasser DL, Weaver VM. Matrix crosslinking forces tumor progression by enhancing integrin signalling. *Cell.* 2009;139(5):891-906. doi: 10.1016/j.cell.2009.10.027.
- Li H, Zeng J, Shen K. PI3K/AKT/mTOR signaling pathway as a therapeutic target for ovarian cancer. *Arch Gynecol Obstet.* 2014; 290(6):1067-78. doi:10.1007/s00404-014-3377-3. PubMed PMID: 25086744.
- Lin AJ, Cosby LA, Shansky CW, Sartorelli AC. Bioreductive alkylating agents: 1. Benzoquinone derivatives. *J Med Chem.* 15: 1247-1252, 1972.
- Lin S, Tsai SC, Lee CC, Wang BW, Liou JY, Shyu KG. Berberine inhibits HIF-1 α expression via enhanced proteolysis. *Mol Pharmacol* 2004; 66:612–619.
- Lin TH, Kuo HC, Chou FP, Lu FJ. Berberine enhances inhibition of glioma tumor cell migration and invasiveness mediated by arsenic trioxide. *BMC Cancer* 2008; 8:58.
- Lind MJ. Principles of cytotoxic chemotherapy. *Medicine*, 2008; 36(1):19–23. doi:10.1016/j.mpmed.2007.10.003.
- Liu B, Wang G, Yang J, Pan X, Yang Z, Linqun Z. Berberine inhibits human hepatoma cell invasion without cytotoxicity in healthy hepatocytes. *PLoS ONE* 2011; 6: 1-10.
- Liu F, Wang P, Jiang X, Tan G, Qiao H, Jiang H, Krissansen GW, Sun X. Antisense hypoxia-inducible factor 1 α gene therapy enhances the therapeutic efficacy of doxorubicin to combat hepatocellular carcinoma. *Cancer Sci.* 2008; 99(10):2055-61. doi: 10.1111/j.1349-7006.2008.00905.x. PubMed PMID: 19016766.

- Liu LF, Desai SD, Li TK, Mao Y, Sun M, Sim SP. Mechanism of action of camptothecin. *Ann N Y Acad Sci.* 2000; 922:1-10. Review. PubMed PMID: 11193884.
- Liu Z, Liu Q, Xu B, Wu J, Guo C, Zhu F, Yang Q, Gao G, Gong Y, Shao C. Berberine induces p53-dependent cell cycle arrest and apoptosis of human osteosarcoma cells by inflicting DNA damage. *Mutat Res.* 2009; 662(1-2):75-83. doi: 10.1016/j.mrfmmm.2008.12.009. PubMed PMID: 19159633.
- Li-Weber M. Targeting apoptosis pathways in cancer by Chinese medicine. *Cancer Lett.* 2013; 332(2):304-12. doi: 10.1016/j.canlet.2010.07.015. Review. PubMed PMID: 20685036.
- Lomax ME, Folkes LK, O'Neill P. Biological consequences of radiation-induced DNA damage: relevance to radiotherapy. *Clin Oncol (R Coll Radiol).* 2013; 25(10):578-85. doi: 10.1016/j.clon. 2013.06.007. Epub 2013 Jul 10. Review. PubMed PMID: 23849504.
- Lomax ME, Folkes LK, O'Neill P. Biological Consequences of Radiation-induced DNA Damage: Relevance to Radiotherapy. *J Clin Oncol.*2013; 25(10):578-585.
- Lowry OH, Rosebrough NJ, Farr AL, Randall RJ. Protein measurement with the Folin phenol reagent. *J Biol Chem.* 1951; 193(1):265-75. PubMed PMID: 14907713.
- Lu RM, Chen MS, Chang DK, Chiu CY, Lin WC, et al. Targeted Drug Delivery Systems Mediated by a Novel Peptide in Breast Cancer Therapy and Imaging. *PLoS ONE*, 2013; 8(6): e66128. doi: 10.1371/journal.pone.0066128.
- Lubbe AS, Bergemann C, Riess H, Schriever F, Reichardt P, Possinger K, Matthias M, Dorken B, Herrmann F, Gurtler R, Hohenberger P, Haas N, Sohr R, Sander B, Lemke AJ, Ohlendorf D, Huhnt W, Huhn D. Clinical experiences with magnetic drug targeting: a phase I study with 4'-epidoxorubicin in 14 patients with advanced solid tumors. *Cancer Res.* 1996; 56:4686-93.
- Ma Y, Manolache S, Denes FS, Thamm DH, Kurzman ID, Vail DM. Plasma synthesis of carbon magnetic nanoparticles and immobilization of doxorubicin for targeted drug delivery. *J Biomater Sci Polym Ed.* 2004; 15(8):1033-49. PubMed PMID: 15461188.
- Mabjeesh NJ, Post DE, Willard MT, Kaur B, Van Meir EG, Simons JW, Zhong H. Geldanamycin induces degradation of hypoxia-inducible factor 1alpha protein via the proteasome pathway in prostate cancer cells. *Cancer Res.*2002; 1;62(9):2478-82. PubMed PMID: 11980636.

- Maeda H, Wu J, Sawa T, Matsumura Y, Hori K. Tumor vascular permeability and the EPR effect in macromolecular therapeutics: a review. *J Control Release*. 2000; 65(1-2):271-84. Review. PubMed PMID: 10699287.
- Maeda H. The enhanced permeability and retention (EPR) effect in tumor vasculature: the key role of tumor-selective macromolecular drug targeting. *Adv Enzyme Regul*. 2001; 41:189-207.
- Magliani W, Conti S, Ciociola T, Giovati L, Zanello PP, Pertinhez T, Spisni A, Polonelli L. Killer peptide: a novel paradigm of antimicrobial, antiviral and immunomodulatory auto-delivering drugs. *Future Med Chem*. 2011; 3(9):1209-31. doi: 10.4155/fmc.11.71. Review. PubMed PMID: 21806382.
- Mahmoudi M, Sant S, Wang B, Laurent S, Sen T. Superparamagnetic iron oxide nanoparticles (SPIONs): Development, surface modification and applications in chemotherapy. *Adv Drug Deliv Rev*. 2011; 63:24–46.
- Majidi S, Zeinali Sehrig F, Samiei M, Milani M, Abbasi E, Dadashzadeh K, Akbarzadeh A. Magnetic nanoparticles: Applications in gene delivery and gene therapy. *Artif Cells Nanomed Biotechnol*. 2016; 44(4):1186-93. doi: 10.3109/
- Mantena SK, Sharma SD, Katiyar SK. Berberine inhibits growth, induces G1 arrest and apoptosis in human epidermoid carcinoma A431 cells by regulating Cdk1-Cdk-cyclin cascade, disruption of mitochondrial membrane potential and cleavage of caspase 3 and PARP. *Carcinogenesis*, 2006a; 27(10):2018-27. PubMed PMID: 16621886.
- Mantena SK, Sharma SD, Katiyar SK. Berberine, a natural product, induces G1-phase cell cycle arrest and caspase-3-dependent apoptosis in human prostate carcinoma cells. *Mol Cancer Ther*. 2006b; 5(2):296-308. PubMed PMID: 16505103.
- Martin F, Nair CKK. Chemosensitization of cisplatin induced mortality of murine tumor cells with sanazole (AK-2123). *Amala Res Bull*. 2010; 30:159-164.
- Masoud GN, Li W. HIF-1 α pathway: role, regulation and intervention for cancer therapy. *Acta Pharm Sin B*. 2015; 5(5):378–389. doi:10.1016/j.apsb.2015.05.007.
- Masunaga S, Uto Y, Nagasawa H, Hori H, Nagata K, Suzuki M, Kinashi Y, Ono K. Evaluation of hypoxic cell radio-sensitizers in terms of radio-sensitizing and repair-inhibiting potential. Dependency on p53 status of tumor cells and the effects on intra-tumor quiescent cells. *Anticancer Res*. 2006; 26(2A):1261-70. PubMed PMID: 16619533.

- Maxwell PH, Dachs GU, Gleadle JM, Nicholls LG, Harris AL, Stratford IJ, Hankinson O, Pugh CW, Ratcliffe PJ. Hypoxia-inducible factor-1 modulates gene expression in solid tumors and influences both angiogenesis and tumor growth. *Proc Natl Acad Sci U S A*. 1997; 94(15):8104-9.
- Maxwell PH, Dachs GU, Gleadle JM, Nicholls LG, Harris AL, Stratford IJ, Hankinson O, Pugh CW, Ratcliffe PJ. Hypoxia-inducible factor-1 modulates gene expression in solid tumors and influences both angiogenesis and tumor growth. *Proc Natl Acad Sci U S A*. 1997; 94(15):8104-9.
- Maxwell PH, Pugh CW, Ratcliffe PJ. The pVHL-HIF-1 system. A key mediator of oxygen homeostasis. *Adv Exp Med Biol* 2001; 502: 365–76.
- McBain SC, Griesenbach U, Xenariou S, Keramane A, Batich CD, Alton EW, Dobson J. Magnetic nanoparticles as gene delivery agents: enhanced transfection in the presence of oscillating magnet arrays. *Nanotechnology*, 2008; 19(40):405102. doi: 10.1088/0957-4484/19/40/405102. PubMed PMID: 21832609.
- McCarthy HO, Yakkundi A, McErlane V, Hughes CM, Keilty G, Murray M, Patterson LH, Hirst DG, McKeown SR, Robson T. Bioreductive GDEPT using cytochrome P450 3A4 in combination with AQ4N. *Cancer Gene Ther*. 2003; 10(1):40-8. PubMed PMID: 12489027.
- McCord JM, Fridovich I. Superoxide dismutase. An enzymic function for erythrocyte hemocuprein. *J Biol Chem*. 1969; 244(22):6049-55. PubMed PMID: 5389100.
- Medina OP, Zhu Y, Kairemo K. Targeted liposomal drug delivery in cancer. *Curr Pharm Des*. 2004; 10(24):2981-9. Review. PubMed PMID: 15379663.
- Meeran SM, Katiyar S, Katiyar SK. Berberine-induced apoptosis in human prostate cancer cells is initiated by reactive oxygen species generation. *Toxicol Appl Pharmacol*. 2008; 229(1):33–43.
- Meng Q, Xia C, Fang J, Rojanasakul Y, Jiang BH. Role of PI3K and AKT specific isoforms in ovarian cancer cell migration, invasion and proliferation through the p70S6K1 pathway. *Cell Signal*, 2006; 18(12):2262–2271.
- Mika D, Guruvayoorappan C. Myeloperoxidase: the yin and yang in tumour progression. *J Exp Ther Oncol*. 2011; 9(2):93-100. Review. PubMed PMID: 21699016.
- Millar BC. Hypoxic cell radiosensitizers as potential adjuvants to conventional chemotherapy for the treatment of cancer. *Biochem.Pharmacol*. 1982; 31(15):2439-45. Review. PubMed PMID: 6751333.

- Minotti G, Menna P, Salvatorelli E, Cairo G, Gianni L. Anthracyclines: molecular advances and pharmacologic developments in antitumor activity and cardiotoxicity. *Pharmacol Rev.* 2004; 56(2):185–229. doi:10.1124/pr.56.2.6. PMID 15169927.
- Mishima F, Takeda S, Izumi Y, Nishijima S. Development of Magnetic Field Control for Magnetically Targeted Drug Delivery System Using a Superconducting Magnet. *IEEE Trans Appl Supercond*, 2007; 17:2303-2306.
- Moghimi SM, Hunter AC, Murray JC. Long-circulating and target-specific nanoparticles: Theory to practice. *Pharmacol Rev.* 2001; 53:283–318.
- Mohindra JK, Rauth AM. Increased cell killing by metronidazole and nitrofurazone of hypoxic compared to aerobic mammalian cells. *Cancer Res.* 36: 930-936, 1976.
- Moore BA, Palcic B, Skarsgard LD. Radiosensitizing and toxic effects of the 2-nitroimidazole Ro-07-0582 in hypoxic mammalian cells. *Radiat Res.* 67: 459-473, 1976.
- Moron MS, Depierre JW, Mannervik B. Levels of glutathione, glutathione reductase and glutathione S-transferase activities in rat lung and liver. *Biochim Biophys Acta.* 1979; 582(1):67-78. PubMed PMID: 760819.
- Mott JD, Werb Z. Regulation of matrix biology by matrix metalloproteinases. *Curr Opin Cell Biol.* 2004;16(5):558-64. Review. PubMed PMID: 15363807; PubMedCentral PMCID: PMC2775446.
- Multhoff G, Botzler C, Wiesnet M, Müller E, Meier T, Wilmanns W, Issels RD. A stress-inducible 72-kDa heat-shock protein (HSP72) is expressed on the surface of human tumor cells, but not on normal cells. *Int J Cancer*, 1995; 61: 272-9.
- Mumenthaler SM, Foo J, Choi NC, Heise N, Leder K, Agus DB, Pao W, Michor F, Mallick P. The Impact of Microenvironmental Heterogeneity on the Evolution of Drug Resistance in Cancer Cells. *Cancer Inform.* 2015; 14(4):19-31. doi: 10.4137/CIN.S19338.
- Murphy MP. How mitochondria produce reactive oxygen species. *Biochemical Journal.* 2009; 417(Pt 1):1-13. doi:10.1042/BJ20081386.
- Murugesan S, Shetty SJ, Noronha OP, Samuel AM, Srivastava TS, Nair CKK, Kothari L. Technetium-99m-cyclam AK 2123: a novel marker for tumor hypoxia. *Appl Radiat Isot.* 2001; 54(1):81-8. PubMed PMID: 11144256.
- Murugesan S, Shetty SJ, Noronha OPD, Samuel AM, Srivastava TS, and Nair CKK. Radiosensitiser for hypoxic tumor imaging. In: Huilgol NG, Nair CKK, Kagiya V.T,

- editors. 'Radiosensitizers in clinical Practice, a contemporary audit. Narosa Publishers, 2000.p.74-86.
- Muzykantov VR. Drug delivery by red blood cells: vascular carriers designed by Mother Nature. *Expert Opin Drug Deliv.* 2010; 7(4):403-427. doi:10.1517/17425241003610633.
- Mykhaylyk O, Sanchez-Antequera Y, Vlaskou D, Cerda MB, Bokharai M, Hammerschmid E, Anton M, Plank C. Magnetic nanoparticle and magnetic field assisted siRNA delivery in vitro. *Methods Mol Biol.*2015; 1218:53-106. doi:10.1007/978-1-4939-1538-5_5. PubMed PMID: 25319646.
- Mykhaylyka O, Vlaskoua D, Tresilwisedb N, Pithayanukulb P, Möllerc W, Plank C. Magnetic nanoparticle formulations for DNA and siRNA delivery. *J Magn Magn Mater*, 2007; 311(1):275–281.
- Nair CKK, Parida DK, Nomura T. Radioprotectors in radiotherapy. *J Radiat Res.*2001; 42(1):21-37.
- Nair GG, Nair CKK. Amelioration of γ -radiation induced genomic insult and oxidative stress in whole body irradiated swiss albino mice by sesamol. *Int J Low Radiat.*2011; 8: 20-34.
- Nair GG, Nair CK. Sanazole directed targeting of silver nanoparticle drugcomplex to tumor mass: a preclinical investigation in murine model. *J Cancer Res Ther.* 2014;10(4):979-84. doi: 10.4103/0973-1482.148705. PubMed PMID:25579540.
- Nakamura H, Ito N, Kotake F, Mizokami Y, Matsuoka T. Tumor-detecting capacity and clinical usefulness of SPIO-MRI in patients with hepatocellular carcinoma. *J Gastroenterol*, 2000; 35 (11): 849–55.
- Neuberger T, Schöpf B, Hofmann H, et al. Superparamagnetic nanoparticles for biomedical applications: Possibilities and limitations of a new drug delivery system. *J Magn Magn Mater.* 2005; 293:483–96.
- Neuss N, Corman M, Boaz HE, Cone NJ. Vinca alkaloids. XI. Structures of leurocristine and vincalukoblastine. *J Am Chem Soc.* 1962; 84:1509–1510.10.1021/ ja00867a049.
- Noguchi Y, Wu J, Duncan R, Strohalm J, Ulbrich K, Akaike T, Maeda H. Early phase tumor accumulation of macromolecules: a great difference in clearance rate between tumor and normal tissues. *Jpn J Cancer Res.* 1998; 89(3):307-14. PubMed PMID: 9600125.

- Nowotny A. Antitumor effects of endotoxins. In: Berry LJ, editor. Handbook of Endotoxin. Vol. 3. Elsevier Science; Amsterdam: 1985. pp. 389–448.
- O'Rourke JF, Dachs GU, Gleadle JM, Maxwell PH, Pugh CW, Stratford IJ, Wood SM, Ratchliffe PJ. Hypoxia response elements. *Oncol Res.*1997; 9: 327–32.
- Odom AL, Hatwig CA, Stanley JS, Benson AM: Biochemical determinants of Adriamycin toxicity in mouse liver, heart and intestine. *Biochem Pharmacol.*1992; 43: 831–836.
- Olson RD, MacDonald JS, van Boxtel CJ, Boerth RC, Harbison RD, Slonim AE, Freeman RW, Oates JA. Regulatory role of glutathione and soluble sulfhydryl groups in the toxicity of Adriamycin. *J Exp Ther.*1980; 215:450–454.
- Orel V, Shevchenko A, Romanov A, Tselepi M, Mitrelias T, Barnes CH, Burlaka A, Lukin S, Shchepotin I. Magnetic properties and antitumor effect of nanocomplexes of iron oxide and doxorubicin. *Nanomedicine.* 2015; 11(1):47-55. doi:10.1016/j.nano.2014.07.007. Epub 2014 Aug 4. PubMed PMID: 25101880.
- Ortiz de Montellano PR. Cytochrome P450-activated prodrugs. *Future Med Chem.*2013; 5(2):213-28. doi:10.4155/fmc.12.197. Review.
- Ozdemir I, Talas ZS, Gok Y, Ates B, Yilmaz I. Changes in tyrosine hydroxylase activity, adrenomedullin (adm) and total RNA levels by treatment of organoselenium compounds in rat hypothalamus exposed to 7,12-dimethyl benzanthracene (DMBA). *Fresenius Environ Bull.*2010; 19(4): 664 – 668.
- Pan GY, Wang GJ, Liu XD, Fawcett JP, Xie YY. The involvement of P-glycoprotein in berberine absorption. *Pharmacol Toxicol.* 2002; 91:193–197.
- Pandey MK, Sung B, Kunnumakkara AB, Sethi G, Chaturvedi MM, Aggarwal BB. Berberine modifies cysteine 179 of I κ B kinase, suppresses nuclear factor- κ B-regulated antiapoptotic gene products, and potentiates apoptosis. *Cancer Res.*2008; 68(13):5370–5379.
- Pankhurst QA, Connolly J, Jones SK, Dobson J. Applications of magnetic nanoparticles in biomedicine. *J Phys D Appl Phys.*2003; 36(13):R167 - R181.
- Parker WB. Enzymology of purine and pyrimidine antimetabolites used in the treatment of cancer. *Chem Rev.* 2009; 109(7):2880–93. doi:10.1021/ cr900028p. PMC 2827868. PMID: 19476376.
- Pasupathy K, Nair CK, Kagiya TV. Effect of a hypoxic radiosensitizer, AK 2123 (Sanazole), on yeast *Saccharomyces cerevisiae*. *J Radiat Res.*2001; 42(2):217-27. PubMed PMID: 11599887.

- Patil JB, Kim J, Jayaprakasha GK. Berberine induces apoptosis in breast cancer cells (MCF-7) through mitochondrial-dependent pathway. *Eur J Pharmacol.* 2010; 645(1–3):70–78.
- Patterson LH, Murray GI. Tumour cytochrome P450 and drug activation. *Curr Pharm Des.* 2002; 8(15):1335–47. Review. PubMed PMID: 12052211.
- Patterson LH. Bio-reductively activated anti-tumor N-oxides: the case of AQ4N, a unique approach to hypoxia activated cancer chemotherapy. *Drug Metab Rev.* 2002; 34: 581–592.
- Peer D, Karp JM, Hong S, Farokhzad OC, Margalit R, Langer R. Nanocarriers as an emerging platform for cancer therapy. *Nat Nanotechnol.* 2007; 2(12):751–60. doi: 10.1038/nano.2007.387. Review. PubMed PMID: 18654426.
- Peng L, Kang S, Yin Z, Jia R, Song X, Li L, Li Z, Zou Y, Liang X, Li L, He C, Ye G, Yin L, Shi F, Lv C, Jing B. Antibacterial activity and mechanism of berberine against *Streptococcus agalactiae*. *Int J Clin Exp Pathol.* 2015; 8(5):5217–23.
- Perche F, Biswas S, Patel NR, Torchilin VP. Hypoxia-Responsive Copolymer for siRNA Delivery. *Methods Mol Biol.* 2016;1372:139–62. doi:10.1007/978-1-4939-3148-4_12. PubMed PMID: 26530922.
- Perche F, Biswas S, Wang T, Zhu L, Torchilin VP. Hypoxia-targeted siRNA delivery. *Angew Chem Int Ed Engl.* 2014 Mar 24;53(13):3362–6. doi: 10.1002/anie.201308368.
- Perrault SD, Walkey C, Jennings T, Fischer HC, Chan WCW. Mediating tumor targeting efficiency of nanoparticles through design. *Nano Lett.*2009; 9:1909–1915.
- Pigram WJ, Fuller W, Hamilton LD. Stereochemistry of intercalation. Intercalation of Daunomycin action. Intercalation of daunomycin with DNA. *Nature.*1972; 235:17–19.
- Pressley RH, Muntz HG, Falkenberry S, Rice LW. Serum lactic dehydrogenase as a tumor marker in dysgerminoma. *Gynecol Oncol.* 1992; 44(3):281–3.
- Prise KM, O'Sullivan JM. Radiation-induced bystander signalling in cancer therapy. *Nat Rev Cancer,*2009; 9(5):351–60. doi: 10.1038/nrc2603. Review. PubMed PMID: 19377507.
- Pugh CW, Ratcliffe PJ. Regulation of angiogenesis by hypoxia: role of the HIF system. *Nat Med.*2003; 9:677–84.
- Qin Y, Pang JY, Chen WH, Zhao ZZ, Liu L, Jiang ZH. Inhibition of DNA topoisomerase I by natural and synthetic mono- and dimeric protoberberine alkaloids. *Chem Biodivers.*2007; 4:481–487.

- Raaphorst GP. Fundamental aspects of hyperthermic biology. In: Field SB and Hand JW (eds.) *An Introduction to the Practical Aspects of Clinical Hyperthermia*, pp. 10–54. Taylor and Francis, London (1990).
- Raghunand N, He X, van Sluis R, Mahoney B, Baggett B, Taylor CW, Paine-Murrieta G, Roe D, Bhujwala ZM, Gillies RJ. Enhancement of chemotherapy by manipulation of tumour pH. *Br J Cancer*, 1999; 80(7):1005-11.
- Rajagopalan R, Kagiya TV, Nair CK. Radiosensitizer sanazole (AK-2123) enhances gamma-radiation-induced apoptosis in murine fibrosarcoma. *J Radiat Res.*2003; 44(4):359-65. PubMed PMID: 15031563.
- Raju HB, Hu Y, Vedula A, Dubovy S R, Goldberg J L.. Evaluation of magnetic micro- and nanoparticle toxicity to ocular tissues. *PLoS One*, 2011; (6):17452-63.
- Ram VJ, Kumari S. Natural products of plant origin as anticancer agents. *Drug News Perspect.* 2001; 14(8):465-82. Erratum in: *Drug News Perspect.* 2001; 14(9):534. PubMed PMID: 12806432.
- Rankin EB, Giaccia AJ. Hypoxic control of metastasis. *Science.* 2016; 352(6282):175-80. doi: 10.1126/science.aaf4405.
- Rao BS, Devi PU. Multimodality treatment using AK-2123, hydralazine, radiation & hyperthermia on a transplantable mouse tumour. *Indian J Med Res.* 1996; 104:182-9. PubMed PMID: 8840657.
- Rauth AM, Mohindra JK, Tannock IF. Activity of mitomycin C for aerobic and hypoxic cells *in vitro* and *in vivo*. *Cancer Res.* 43: 4154-4158, 1983.
- Richard CD, Roxana ZW, Paul BN, John D, Young E, David MO. Cytolysis mediated by ionophores and pore-forming agents: role of intracellular calcium in apoptosis. *FASEB J* 1994; 8: 237-246.
- Richard CD, Roxana ZW, Paul BN, John D, Young E, David MO. Cytolysis mediated by ionophores and pore-forming agents: role of intracellular calcium in apoptosis. *FASEB J.* 1994; 8: 237-46.
- Riemer J, Hoepken HH, Czerwinska H, Robinson SR and Dringen R. Colorimetric ferrozine-based assay for the quantitation of iron in cultured cells. *Anal Biochem.* 2004; 331: 370–375.
- Ritter JA, Ebner AD, Daniel KD, Stewart KL. Application of high gradient magnetic separation principles to magnetic drug targeting. *J Magn Magn Mater*, 2004; 280: 184–201.

- Rivera GP, Huhn D, del Mercato LL, Sasse D, Parak WJ. Nanopharmacy: Inorganic nanoscale devices as vectors and active compounds. *Pharmacol Res*, 2010; 62:115-25.
- Rockwell S, Dobrucki IT, Kim EY, Marrison ST, Vu VT. Hypoxia and radiation therapy: past history, on-going research, and future promise. *Curr Mol Med*. 2009; 9(4):442-58. PubMed PMID: 19519402.
- Romero MR, Efferth T, Serrano MA, Castano B, Macias RI, Briz O, et al. Effect of artemisinin/artesunate as inhibitors of hepatitis B virus production in an 'in vitro' replicative system. *Antiviral Res*. 2005; 68:75–83.
- Rudgea SR, Kurtza TL, Vesselya CR, Catteralla LG, Williamsonb DL. Preparation, characterization, and performance of magnetic iron-carbon composite microparticles for chemotherapy. *Biomaterials*, 2000; 21:1411–1420.
- Rungsitiyakorn A, Wilairat P, Panijpan B. On the pH dependence of binding of berberine to DNA. *J Pharm Pharmacol*. 1981; 33(2):125-7. PubMed PMID: 6111598.
- Saiyed ZM, Ramchand CN, Telang SD. Isolation of genomic DNA using magnetic nanoparticles as a solid-phase support. *J Phys Condens Matter*. 2008; 20(20):204153. doi: 10.1088/0953-8984/20/20/204153. PubMed PMID: 21694281.
- Sandau KB, Fandrey J and Bruˆne B. Accumulation of HIF-1a under the influence of nitric oxide. *Blood* 2001; 97(4):1009-1015.
- Sandeep D, Nair CKK, Protection of DNA and membrane from γ -radiation induced damage by the extract of *Acorus calamus* Linn.-An in vitro study. *Environ Toxicol Phar* 2010; 29: 302-307.
- Sandeep D, Nair CKK. Protection of DNA and membrane from γ -radiation induced damage by the extract of *Acorus calamus* Linn.-an in vitro study. *Environ Toxicol Phar*. 2010; 29: 302-307.
- Sandoval J, Esteller M. Cancer epigenomics: beyond genomics. *Curr Opin Genet Dev*. 2012; 22(1):50-5. doi: 10.1016/j.gde.2012.02.008. Epub 2012 Mar 6. Review. PubMed PMID: 22402447.
- Sathyavathi GV, Gupta AK, Tandon N, et al. Medicinal plants of India. Vol. 2. New Delhi (India): Indian Council of Medical Research; 1987. p.230–9
- Schepetkin IA, Cherdyntseva NV, Kagiya VT. Sanazole as substrate of xanthine oxidase and microsomal NADPH/cytochrome P450 reductase. *Pathophysiology*, 2001; 8(2):119-127. PubMed PMID: 11720808.

- Schmittgen TD, Livak KJ. Analyzing real-time PCR data by the comparative C(T) method. *Nat Protoc.* 2008; 3(6):1101-8. PubMed PMID: 18546601.
- Schwartzburd PM, Lankin VZ. Lipoproteins in hypoxic tumor cells as traps of free radicals. *Med Oncol.* 1994; 11(3-4):101-10. PubMed PMID: 7633829.
- Scott AM, Wolchok JD, Old LJ. Antibody therapy of cancer. *Nat Rev Cancer*, 2012; 12(4): 278–87. doi:10.1038/nrc3236. PMID 22437872.
- Semenza GL, Neefelt MK, Chi SM, Antonarakis SE. Hypoxia-inducible nuclear factors bind to an enhancer element located 3' to the human erythropoietin gene. *Proc Natl Acad Sci U S A.* 1991;88(13):5680-4.
- Semenza GL. HIF-1 mediates metabolic responses to intratumoral hypoxia and oncogenic mutations. *J Clin Invest.* 2013; 123(9):3664–3671.
- Semenza GL. Hypoxia, clonal selection, and the role of HIF-1 in tumour progression. *Crit Rev Biochem Mol Biol.* 2000; 35(2):71-103. Review. PubMed PMID: 10821478.
- Semenza GL. Hypoxia-inducible factor 1: Control of oxygen homeostasis in health and disease. *Pediatr Res.*2001; 49:614-617.
- Sergeev PV, Semeikin AV, Fedotcheva TA, Samoilikov RV, Kamernitskii A V, Levina I S, et al. Combined Action of Doxorubicin and Gestagens on doxorubicin sensitive and doxorubicin resistant MCF-7 cells. *B Exp Biol Med.* 2003; 5: 460-3.
- Sermeus A, Genin M, Maincent A, Fransolet M, Notte A, Leclere L, Riquier H, Arnould T, Michiels C. Hypoxia-induced modulation of apoptosis and BCL-2 family proteins in different cancer cell types. *PLoS One.* 2012; 7(11): e47519. doi:10.1371/journal.pone.0047519.
- Sethi T, Rintoul RC, Moore SM, MacKinnon AC, Salter D, Choo C, Chilvers ER, Dransfield I, Donnelly SC, Strieter R, Haslett C. Extracellular matrix proteins protect small cell lung cancer cells against apoptosis: a mechanism for small cell lung cancer growth and drug resistance in vivo. *Nat Med.* 1999; 5(6):662-8.
- Shain KH, Dalton WS. Cell adhesion is a key determinant in de novo multidrug resistance (MDR): new targets for the prevention of acquired MDR. *Mol Cancer Ther* 2001; 1: 69 – 78.
- Shapiro GI, Koestner DA, Matranga CB, Rollins BJ. Flavopiridol induces cell cycle arrest and p53-independent apoptosis in non-small cell lung cancer cell lines. *Clin Cancer Res.* 1999; 5(10):2925-38. PubMed PMID: 10537362.

- Sharkey RM, Goldenberg DM. Cancer radioimmunotherapy. *Immunotherapy*. 2011; 3(3):349-70. doi: 10.2217/imt.10.114. Review. PubMed PMID: 21395378.
- Shay JW, Keith WN. Targeting telomerase for cancer therapeutics. *British Journal of Cancer*. 2008; 98(4):677-683. doi:10.1038/sj.bjc.6604209.
- Sheehan JP, Shaffrey ME, Gupta B, Lerner J, Rich JN, Park DM. Improving the radiosensitivity of radioresistant and hypoxic glioblastoma. *Future Oncol*. 2010; 6(10):1591-601. doi: 10.2217/fon.10.123. Review. PubMed PMID: 21062158.
- Shen G, Jeong WS, Hu R, Kong AN. Regulation of Nrf2, NF-kappaB, and AP-1 signaling pathways by chemopreventive agents. *Antioxid Redox Signal*. 2005; 7(11-12):1648-63. Review. PubMed PMID: 16356127.
- Shibamoto Y, Nishimoto S, Mi F, Sasai K, Kagiya T, Abe M. Evaluation of various types of new hypoxic cell sensitizers using the EMT6 single cell-spheroid-solid tumour system. *Int J Radiat Biol Relat Stud Phys Chem Med*. 1987; 52(3):347-57. PubMed PMID: 3497891.
- Shibamoto Y, Sakano K, Kimura R, Nishidai T, Nishimoto S, Ono K, Kagiya T, Abe M. Radiosensitization *in vitro* and *in vivo* by 3-nitrotriazoles. *Int J Radiat Oncol Biol Phys*. 1986; 12(7):1063-6. PubMed PMID: 3744928.
- Shibata T, Giaccia AJ, Brown JM. Hypoxia-inducible regulation of a prodrug-activating enzyme for tumor-specific gene therapy. *Neoplasia*, 2002; 4: 40-48.
- Shundo C, Zhang H, Nakanishi T, Osaka T. Cytotoxicity evaluation of magnetite (Fe₃O₄) nanoparticles in mouse embryonic stem cells. *Colloids Surf B Biointerfaces*, 2012; 97: 221-225.
- Siddik ZH. Mechanisms of Action of Cancer Chemotherapeutic Agents: DNA-Interactive Alkylating Agents and Anti-tumour Platinum-Based Drugs. John Wiley & Sons, Ltd. 2005. doi:10.1002/0470025077.chap84b.
- Singh T, Vaid M, Katiyar N, Sharma S, Katiyar SK. Berberine, an isoquinoline alkaloid, inhibits melanoma cancer cell migration by reducing the expressions of cyclooxygenase-2, prostaglandin E and prostaglandin E receptors. *Carcinogenesis*, 2011; 32(1):86-92.
- Singhal KC. Anthelmintic activity of berberine hydrochloride against *Syphacia obvelata* in mice. *Indian J Exp Biol*. 1976; 14:345-347.

- Sminia P, van der Zee J, Wondergem J, Haveman J. Effect of hyperthermia on the central nervous system: a review. *Int J Hyperthermia*. 1994; 10(1):1-30. Review. PubMed PMID: 8144981.
- Sobell HM. Actinomycin and DNA transcription. *Proc Natl Acad Sci USA*, 1985; 82(16):5328–31. doi:10.1073/pnas.82.16.5328. PMID: 2410919.
- Sogawa K, Numayama-Tsuruta K, Ema M, Abe M, Abe H, Fujii-Kuriyama Y. Inhibition of hypoxia-inducible factor 1 activity by nitric oxide donors in hypoxia. *Proc Natl Acad Sci U S A*. 1998; 95(13):7368-73.
- Sonavane G, Tomoda K, Makino K. Biodistribution of colloidal gold nanoparticles after intravenous administration: effect of particle size. *Colloids Surf B*. 2008; 66: 274–280.
- Song M, Liu T, Shi C, Zhang X, Chen X. Bioconjugated Manganese Dioxide Nanoparticles Enhance Chemotherapy Response by Priming Tumor-Associated Macrophages toward M1-like Phenotype and Attenuating Tumor Hypoxia. *ACS Nano*. 2016; 10(1):633-47. doi: 10.1021/acsnano.5b06779.
- Song X, Liu X, Chi W, Liu Y, Wei L, Wang X, Yu J. Hypoxia-induced resistance to cisplatin and doxorubicin in non-small cell lung cancer is inhibited by silencing of HIF-1alpha gene. *Cancer Chemother Pharmacol*. 2006; 58(6):776-84.
- Sophie L, Delphine F, Marc P, Alain R, Caroline R, Luce VE, Robert NM. Magnetic iron oxide nanoparticles: synthesis, stabilization, vectorization, physicochemical characterization, and biological applications. *Chem Rev*. 2008; 108:2064-2110.
- Sperker B, Werner U, Mürdter TE, Tekkaya C, Fritz P, Wacke R, Adam U, Gerken M, Drewelow B, Kroemer HK. Expression and function of beta-glucuronidase in pancreatic cancer: potential role in drug targeting. *Naunyn Schmiedebergs Arch Pharmacol*. 2000; 362(2):110-5. PubMed PMID: 10961372.
- Sreeja S, Nair CK. Anticancer Property of Iron Oxide Nanoparticle-Drug Complexes: An In Vitro Study. *J Environ Pathol Toxicol Oncol*. 2015b; 34(3):183-9.
- Sreeja S, Nair CKK. Chemo-directed specific targeting of nanoparticle-doxorubicin complexes to tumor in animal model. *J Drug Deliv Sci Technol*. 2016; 31:167-175.
- Sreeja S, Nair CKK. Magnetic nanoparticles directed delivery of Berberine- a cytotoxic phytochemical, for tumor control. 2015a. *Adv Sci Eng Med*. 6:53-61.
- Sreeja S, Nair CKK. Preclinical investigations on antineoplastic activity of Ironoxide nanoparticle – drug complexes. *Adv Mat Res*. 2015c; 1086:43-49. (doi:10.4028/www.scientific.net/AMR.1086.43).

- Strober W. Trypan blue exclusion test of cell viability. In: Current Protocols in Immunology: Wiley Online Library; 1997. p. A.3B.1-A.3B.2.
- Sullivan R, Pare GC, Frederiksen LJ, Semenza GL, Graham CH. Hypoxia-induced resistance to anticancer drugs is associated with decreased senescence and requires hypoxia-inducible factor-1 activity. *Mol Cancer Ther.*2008; 7:1961–1973.
- Sun C, Lee JS, Zhang M. Magnetic nanoparticles in MR imaging and drug delivery. *Adv Drug Deliv Rev.* 2008; 60(11):1252-65. doi:10.1016/j.addr.2008.03.018. Review. PubMed PMID: 18558452; PubMed Central PMCID: PMC2702670.
- Sun X, Kanwar JR, Leung E, Lehnert K, Wang D, Krissansen GW. Gene transfer of antisense hypoxia inducible factor-1 α enhances the therapeutic efficacy of cancer immunotherapy. *Gene Ther.*2001; 8: 638–645.
- Sun Y, Xun K, Wang Y, Chen X. A systematic review of the anticancer properties of berberine, a natural product from Chinese herbs. *Anticancer Drugs.*2009; 20(9):757-69. doi: 10.1097/CAD.0b013e328330d95b. Review. PubMed PMID: 19704371.
- Svoboda GH. Alkaloids of *Vinca rosea* (*Catharanthus roseus*). IX. Extraction and characterization of leurosidine and leurocristine. *Lloydia*, 1961; 24:173–178.
- Tahervand A, Mahmoudi M, Roushandeh AM. Digoxin effectively decreased proliferation of liver cancer cell line. *Focus Sci.* 2016; 2: 1–6.
- Takeda S, Mishima F, Fujimoto S, Izumi Y, Nishijima S. Development of magnetically targeted drug delivery system using superconducting magnet. *J Magn Magn Mater*, 2007; 311:367–371.
- Takemura G, Fujiwara H: Doxorubicin-induced cardiomyopathy from the cardiotoxic mechanisms to management. *Prog Cardiovasc Dis.*2007; 49: 330–352.
- Talas ZS, Bayraktar N, Ozdemir I, Gok Y, Yilmaz I. The effects of synthetic organoselenium compounds on nitric oxide in DMBA-induced rat liver. *J Environ Biol.*2009; 30(4):591-3. PubMed PMID: 20120501.
- Talas ZS, Ozdemir I, Gok Y, Ates B, Yilmaz I. Role of selenium compounds on tyrosine hydroxylase activity, adrenomedullin and total RNA levels in hearts of rats. *Regul Pept.* 2010; 159(1-3):137-41. doi: 10.1016/j.regpep.2009.08.009. PubMed PMID: 19706312.
- Talks KL, Turle H, Gatter KC, Maxwell PH, Pugh CW, Ratcliffe PJ, Harris AL. The expression and distribution of the hypoxia-inducible factors HIF-1 α and HIF-2 α in normal human tissues, cancers, and tumor-associated macrophages. *Am J Pathol.*2000; 157(2):411-421.

- Tannock I. Cell kinetics and chemotherapy: a critical review. *Cancer Treat Rep.* 1978; 62(8):1117-33. PubMed PMID: 356975.
- Tannock IF, Rotin D. Acid pH in tumors and its potential for therapeutic exploitation. *Cancer Res.* 1989; 49:4373 – 84.
- Tannock IF. The relation between cell proliferation and the vascular system in a transplanted mouse mammary tumour. *Br J Cancer*, 1968; 22 : 258 – 73.
- Teicher BA, Holden SA, al-Achi A, Herman TS. Classification of antineoplastic treatments by their differential toxicity toward putative oxygenated and hypoxic tumor subpopulations *in vivo* in the FSaIIC murine fibrosarcoma. *Cancer Res.* 1990; 50: 3339-44.
- Thambi T, Deepagan VG, Yoon HY, Han HS, Kim SH, Son S, Jo DG, Ahn CH, Suh YD, Kim K, Kwon IC, Lee DS, Park JH. Hypoxia-responsive polymeric nanoparticles for tumor-targeted drug delivery. *Biomaterials*, 2014; 35(5):1735-43. doi:10.1016/j.biomaterials.2013.11.022.
- Thefeld W, Hoffmeister H, Busch EW, Koller PU, Vollmar J. Reference values for the determination of GOT, GPT, and alkaline phosphatase in serum with optimal standard methods (author's transl) [Article in German]. *Dtsch Med Wochenschr.* 1974; 99(8):343-344.
- Thomas DS, Kenneth J L. Analyzing real-time PCR data by the comparative CT method. *Nat Protoc*, 2008; 3(6):1101-1108.
- Thomlinson RH and Gray LH. The histological structure of some human lung cancers and the possible implications for radiotherapy. *Br J Cancer*, 1955; 9:539-549.
- Tran TM, Temkin V, Shi B, Pagliari L, Daniel S, Ferran C, Pope RM. TNFalpha-induced macrophage death via caspase-dependent and independent pathways. *Apoptosis.* 2009; 14(3):320-32. doi: 10.1007/s10495-009-0311-4. PubMed PMID: 19152111.
- Trédan O, Galmarini CM, Patel K, Tannock IF. Drug resistance and the solid tumor microenvironment. *J Natl Cancer Inst.* 2007; 99:1441– 54.
- Treuel L, Brandholt S, Maffre P, Wiegele S, Shang L, Nienhaus GU. Impact of protein modification on the protein corona on nanoparticles and nanoparticle-cell interactions. *ACS Nano.* 2014; 8:503–513.
- Trinh QT, Austin EA, Murray DM, Knick VC, Huber BE. Enzyme/prodrug gene therapy: comparison of cytosine deaminase/5-fluorocytosine versus thymidine

- kinase/ganciclovir enzyme/prodrug systems in a human colorectal carcinoma cell line. *Cancer Res.* 1995; 55(21):4808-12. PubMed PMID: 7585511.
- Tsai SC, Lee CC, Wang BW, Liou JY, Shyu KG. Berberine inhibits HIF-1 α expression via enhanced proteolysis. *Mol Pharmacol* 2004; 66:612–619.
- Tsang CM, Lau EP, Di K, Cheung PY, Hau PM, Ching YP, Wong YC, Cheung AL, Wan TS, Tong Y, Tsao SW, Feng Y. Berberine inhibits Rho GTPases and cell migration at low doses but induces G2 arrest and apoptosis at high doses in human cancer cells. *Int J Mol Med.* 2009; 24(1):131-8. PubMed PMID: 19513545.
- Ulukan H, Swaan PW. Camptothecins: a review of their chemotherapeutic potential. *Drugs.* 2002; 62(14):2039-57. Review. PubMed PMID: 12269849.
- Vaupel P, Kallinowski F, Okunieff P. Blood flow, oxygen and nutrient supply, and metabolic microenvironment of human tumors: a review. *Cancer Res.* 1989; 49:6449 – 65.
- Veronese FM, Pasut G. PEGylation, successful approach to drug delivery. *Drug Discov Today,* 2005; 10(21):1451–1458.
- Voulgaris S, Partheni M, Karamouzis M, Dimopoulos P, Papadakis N, Kalofonos HP. Intratumoral doxorubicin in patients with malignant brain gliomas. *Am J Clin Oncol.* 2002; 25(1):60-4. PubMed PMID: 11823699.
- Walkey CD, Olsen JB, Guo H, Emili A, Chan WCW. Nanoparticle size and surface chemistry determine serum protein adsorption and macrophage uptake. *J Am Chem Soc.* 2012; 134:2139–2147.
- Wall ME, Wani MC, Cook CE, Palmer KH, McPhail AT, Sim GA. Plant antitumor agents. I. The isolation and structure of camptothecin, a novel alkaloidal leukemia and tumor inhibitor from *Camptotheca acuminata*. *J Am Chem Soc.* 1966; 88:3888–890.10.1021/ja00968a057.
- Walter M. *Micro Chem Jm* 1980; 15:231.
- Wang GL, Jiang BH, Rue EA, Semenza GL. Hypoxia-inducible factor 1 is a basic-helix-loop-helix-PAS heterodimer regulated by cellular O₂ tension. *Proc Natl Acad Sci USA.* 1995b; 92(12):5510–5514. doi: 10.1073/pnas.92.12.5510.
- Wang GL, Semenza GL. Purification and characterization of hypoxia-inducible factor 1. *J Biol Chem.* 1995; 270(3):1230–1237. doi:10.1074/jbc.270.3.1230.

- Wang W, Erbe AK, Hank JA, Morris ZS, Sondel PM. NK Cell-Mediated Antibody-Dependent Cellular Cytotoxicity in Cancer Immunotherapy. *Front Immunol.*2015; 6:368. doi: 10.3389/fimmu.2015.00368. Review. PubMed PMID: 26284063.
- Wang YX, Hussain SM, Krestin GP. Superparamagnetic iron oxide contrast agents: physicochemical characteristics and applications in MR imaging. *Eur Radiol.* 2001; 11(11):2319-31. DOI: 10.1007/s003300100908. PMID: 11702180.
- Wanga X, Gub H, Yangc Z. The heating effect of magnetic fluids in an alternating magnetic field. *J Magn Magn Mater*, 2005; 293:334–340.
- Wani MC, Taylor HLawrence, Wall ME, Coggon P, McPhail AT. Plant antitumor agents. VI. Isolation and structure of taxol, a novel antileukemic and antitumor agent from *Taxus brevifolia*. *J Am Chem Soc.*1971; 93:2325–2327.10.1021/ja00738a045.
- Warburg O. On the origin of cancer cells. *Science*, 1956; 123:309 – 14.
- Weaver VM, Lelièvre S, Lakins JN, Chrenek MA, Jones JC, Giancotti F, Werb Z, Bissell MJ. beta4 integrin-dependent formation of polarized three-dimensional architecture confers resistance to apoptosis in normal and malignant mammary epithelium. *Cancer Cell*, 2002; 2(3):205-16.
- Wei Bhaar D, Grossau E, Faderal B. Normal ranges of alpha- HBDH, LDH, AP and LAP as measured with substrate- optimized test charges. *Med. Welt.*1975; 26: 387- 392.
- Wei Y, Zhou F, Zhang D, Chen Q, Xing D. A graphene oxide based smart drug delivery system for tumor mitochondria-targeting photodynamic therapy. *Nanoscale.* 2016; 8(6):3530-8. doi: 10.1039/c5nr07785k. Epub 2016 Jan 22. PubMed PMID: 26799192.
- Weiner LM, Surana R, Wang S. Monoclonal antibodies: versatile platforms for cancer immunotherapy. *Nat Rev Immunol.*2010; 10(5):317-27. doi:10.1038/nri2744. Review. PubMed PMID: 20414205; PubMed Central PMCID: PMC3508064.
- Weishaar HD. The photometric determination of LDH. *Med Welt.*1975; 26:387.
- Weisshaar D, Gossrau E, Faderl B. Normal ranges of alpha-HBDH, LDH, AP, and LAP as measured with substrate-optimized test charges. *Med Welt.*1975; 26:387-92.
- Werner D, Nagraj G H, Ranapala SJ, Noor-I-Alam Kizilbash, Sait Okkan, Tsutomu V Kagiya, et al. AK-2123 (Sanazole) as a radiation sensitizer in the treatment of stage III cancer cervix: Initial results of an IAEA multicentre randomized trial. *J Can Res Ther* 2005; 1:75-78.
- Wilson MW, Kerlan RK Jr, Fidelman NA, Venook AP, LaBerge JM, Koda J, Gordon RL. Hepatocellular carcinoma: regional therapy with a magnetic targeted carrier bound to

- doxorubicin in a dual MR imaging/ conventional angiography suite--initial experience with four patients. *Radiology*, 2004; 230(1):287-93. PubMed PMID: 14695402.
- Wilson WR: Tumour hypoxia: challenges for cancer chemotherapy. In: Waring M J, Ponder BAJ (eds.) *Cancer Biology and Medicine* (vol 3). Kluwer Academic Publishers, Lancaster, 1992, pp 87-131.
- Wing DA, Talley GD, Storch TG. Oxygen concentration regulates EGF-induced proliferation and EGF-receptor down regulation. *Biochem Biophys Res Commun*.1988; 153:952-958.
- Winkelman J, Cannon DC, Jacobs SL. Liver function tests, including bile pigments, Henry RJ DC Cannon JW. Winkelman (Eds.), In: *Clinical Chemistry- Principles and Techniques*, Harper & Row, Hagerstown, MD, 1974: 1003-1109.
- Witt I, Trendelenburg C. Joint study to establish reference values for clinical chemical parameters in childhood (author's transl). *J Clin Chem Clin Biochem*.1982; 20: 235-42.
- Wozniak MA, Desai R, Solski PA, Der CJ, Keely PJ. ROCK-generated contractility regulates breast epithelial cell differentiation in response to the physical properties of a three-dimensional collagen matrix. *J Cell Biol*. 2003; 163(3): 583-95.
- Wu HL, Hsu CY, Liu WH, Yung BY. Berberine-induced apoptosis of human leukemia HL-60 cells is associated with down-regulation of nucleophosmin/B23 and telomerase activity. *Int J Cancer*. 1999; 81(6):923-9. PubMed PMID: 10362140.
- Wu Y, Li JQ, Kim YJ, Wu J, Wang Q, Hao Y. *In vivo* and *in vitro* antiviral effects of berberine on influenza virus. *Chin J Integr Med*. 2011; 17(6):444-52. doi: 10.1007/s11655-011-0640-3.
- Wust P, Hildebrandt B, Sreenivasa G, Rau B, Gellermann J, Riess H, Felix R, Schlag PM. Hyperthermia in combined treatment of cancer. *Lancet Oncol*.2002; 3(8):487-97. Review. PubMed PMID: 12147435.
- Xiao H, Tong R, Ding C, Lv Z, Du C, Peng C, Cheng S, Xie H, Zhou L, Wu J, Zheng S. γ -H2AX promotes hepatocellular carcinoma angiogenesis via EGFR/HIF-1 α / VEGF pathways under hypoxic condition. *Oncotarget*.2015; 6(4): 2180-92.
- Xu H, Lv M, Tian X. A review on hemisynthesis, biosynthesis, biological activities, mode of action, and structure-activity relationship of podophyllotoxins: 2003-2007. *Current Med Chem*. 2009; 16 (3): 327–349. doi:10.2174/092986709787002682.

- Xu Y, Goldkorn A. Telomere and Telomerase Therapeutics in Cancer. *Genes (Basel)*. 2016; 7(6). doi:10.3390/genes7060022. Review. PubMed PMID: 27240403; PubMed Central PMCID: PMC4929421.
- Yang HW, Hua MY, Liu HL, Huang CY, Wei KC. Potential of magnetic nanoparticles for targeted drug delivery. *Nanotechnol Sci Appl*.2012; 5:73-86. doi:10.2147/NSA.S35506.
- Yao X, Panichpisal K, Kurtzman N, Nugent K. Cisplatin Nephrotoxicity: A Review. *Am J Med Sci*. 2007; 334(2):115–124.
- Yonenaga Y, Mori A, Onodera H, Yasuda S, Oe H, Fujimoto A, Tachibana T, Imamura M. Absence of smooth muscle actin-positive pericyte coverage of tumour vessels correlates with hematogenous metastasis and prognosis of colorectal cancer patients. *Oncology*, 2005; 69(2):159-66. Epub 2005 Aug 24. PubMed PMID:16127287.
- Yu DY, Zhao QL, Wei ZL, Shehata M, Kondo T. Enhancement of hyperthermia-induced apoptosis by sanazole in human lymphoma U937 cells. *Int J Hyperthermia*, 2009; 25(5):364-73. doi: 10.1080/02656730902967418. PubMed PMID: 19551546.
- Yu DY, Zhao QL, Wei ZL, Shehata M, Kondo T. Enhancement of hyperthermia-induced apoptosis by sanazole in human lymphoma U937 cells. *Int J Hyperthermia*, 2009; 25(5):364-73. doi: 10.1080/02656730902967418. PubMed PMID:19551546.
- Yu FS, Yang JS, Lin HJ, Yu CS, Tan TW, Lin YT, Lin CC, Lu HF, Chung JG. Berberine inhibits WEHI-3 leukemia cells in vivo. *In Vivo*, 2007; 21(2):407-12. PubMed PMID: 17436595.
- Zagorevskii D, Song M, Breneman C, Yuan Y, Fuchs T, Gates KS, Greenlief CM. A mass spectrometry study of tirapazamine and its metabolites. insights into the mechanism of metabolic transformations and the characterization of reaction intermediates. *J Am Soc Mass Spectrom*. 2003; 14(8):881-92. PubMed PMID:12892912.
- Zellmer S, Cevc G. Tumor targeting in vivo by means of thermolabile fusogenic liposomes. *J Drug Target*. 1996; 4(1):19-29. PubMed PMID: 8798875.
- Zeman EM, Brown JM, Lemmon MJ, Hirst VK, Lee WW. SR-4233: a new bioreductive agent with high selective toxicity for hypoxic mammalian cells. *Int J Radiat Oncol Biol Phys*.1986; 12: 1239–1242.
- Zhang HJ, Zhao W, Venkataraman S, Robbins ME, Buettner GR, Kregel KC, Oberley LW. Activation of matrix metalloproteinase-2 by overexpression of manganese superoxide dismutase in human breast cancer MCF-7 cells involves reactive oxygen species. *J Biol Chem*.2002; 277(23):20919-26. PubMed PMID: 11929863.

Zhang X, Gu L, Li J, Shah N, He J, Yang L, Hu Q, Zhou M. Degradation of MDM2 by the interaction between berberine and DAXX leads to potent apoptosis in MDM2-overexpressing cancer cells. *Cancer Res.* 2010; 70(23):9895-904. doi:10.1158/0008-5472.CAN-10-1546. PubMed PMID: 20935220.

Zhao T, Ren H, Jia L, Chen J, Xin W, Yan F, Li J, Wang X, Gao S, Qian D, Huang C, Hao J. Inhibition of HIF-1 α by PX-478 enhances the anti-tumor effect of gemcitabine by inducing immunogenic cell death in pancreatic ductal adenocarcinoma. *Oncotarget*, 2015; 6(4):2250-62. PubMed PMID: 25544770.

Zhong H, De Marzo AM, Laughner E, Lim M, Hilton DA, Zagzag D, Buechler P, Isaacs WB, Semenza GL, Simons JW. Overexpression of hypoxia-inducible factor 1 α in common human cancers and their metastases. *Cancer Res.*1999; 59(22): 5830-5835. PubMed PMID: 10582706.

¹<http://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=45301>