

REFERENCES

- Abari, A. H., Rourani, H. A., Ghasemi, S. M., Kim, H., & Kim, Y.-G. (2021). Investigation of antioxidant and anticancer activities of unsaturated oligo-galacturonic acids produced by pectinase of *Streptomyces hydrogenans* YAM1. *Scientific Reports*, *11*, 8491.
- Abdel-Aziz, H. A., Ghabbour, H. A., Eldehna, W. M., Al-Rashood, S. T. A., Al-Rashood, K. A., Fun, H.-K., ... Al-Dhfyhan, A. (2015). 2-((Benzimidazol-2-yl)thio)-1-arylethan-1-ones: Synthesis, crystal study and cancer stem cells CD133 targeting potential. *European Journal of Medicinal Chemistry*, *104*, 1–10.
- Adamsen, B. L., Kravik, K. L., & De Angelis, P. M. (2011). DNA damage signaling in response to 5-fluorouracil in three colorectal cancer cell lines with different mismatch repair and TP53 status. *International Journal of Oncology*, *39*(3), 673–682.
- Adhikari, H. S., & Yadav, P. N. (2018). Anticancer Activity of Chitosan, Chitosan Derivatives, and Their Mechanism of Action. *International Journal of Biomaterials*, *2018*, 1–29.
- Ahmed, D., Eide, P. W., Eilertsen, I. A., Danielsen, S. A., Eknaes, M., Hektoen, M., Lind, G. E., & Lothe, R. A. (2013). Epigenetic and genetic features of 24 colon cancer cell lines. *Oncogenesis*, *2*(9), e71.
- Akahani, S., Nangia-Makker, P., Inohara, H., Kim, H. R., & Raz, A. (1997). Galectin-3: a novel antiapoptotic molecule with a functional BH1 (NWGR) domain of Bcl-2 family. *Cancer Research*, *57*, 5272–5276.
- Asakawa, T., Tsujii, M., Kondo, J., Hayashi, Y., Ying, J., Lu, Y., ... Takehara, T. (2014). 5-FU resistance abrogates the amplified cytotoxic effects induced by inhibiting checkpoint kinase 1 in p53-mutated colon cancer cells. *International Journal of Oncology*, *46*(1), 63–70.
- Alcolea, V., Plano, D., Karelia, D. N., Palop, J. A., Amin, S., Sanmartín, C., & Sharma, A. K. (2016). Novel seleno- and thio-urea derivatives with potent *in vitro* activities against several cancer cell lines. *European Journal of Medicinal Chemistry*, *113*, 134–144.
- Aponte, J. C., Vaisberg, A. J., Castillo, D., Gonzalez, G., Estevez, Y., Arevalo, J., ... Hammond, G. B. (2010). Trypanoside, anti-tuberculosis, leishmanicidal, and cytotoxic activities of tetrahydrobenzothienopyrimidines. *Bioorganic & Medicinal Chemistry*, *18*(8), 2880–2886.
- Attallah, O. A., Shetta, A., Elsishiny, F., & Mamdouh, W. (2020). Essential oil loaded pectin/chitosan nanoparticles preparation and optimization via Box–Behnken design against MCF-7 breast cancer cell lines. *RSC Advances*, *10*, 8703.
- Atuma, C., Strugala, V., Allen, A., & Holm, L. (2001). The adherent gastrointestinal mucus gel layer: thickness and physical state in vivo. *American journal of physiology. Gastrointestinal and Liver Physiology*, *280*(5), G922–G929.
- Avivi-Green, C., Polak-Charcon, S., Madar, Z., & Schwartz, B. (2000). Dietary regulation and localization of apoptosis cascade proteins in the colonic crypt. *Journal of Cellular Biochemistry*, *77*(1), 18–29.
- Azuma, K., Osaki, T., Minami, S., & Okamoto, Y. (2015). Anticancer and Anti-Inflammatory Properties of Chitin and Chitosan Oligosaccharides. *Journal of Functional Biomaterials*, *6*(1), 33–49.
- Bagheri, E., Hajiaghaalipour, F., Nyamathulla, S., & Salehen, N. (2018). The apoptotic effects of Brucea javanica fruit extract against HT29 cells associated with p53 upregulation and inhibition of NF-κB translocation. *Drug Design, Development and Therapy*, *12*, 657–671.
- Bahn, Y. E., Bak, S. S., Ha, J. K., Kim, S. H., Moon, S. H., & Park, K. Y. (2008). Anticancer Effect of Chitosan in HT-29 Human Colon Cancer Cells. *Journal of Cancer Prevention*, *13*, 284–291.
- Barrow, H., Rhodes, J. M., & Yu, L. G. (2011). The role of galectins in colorectal cancer progression. *International Journal of Cancer*, *129*(1), 1–8.
- Belali, N., Wathoni, N., & Muchtaridi, M. (2019). Advances in orally targeted drug delivery to colon. *Journal of Advanced Pharmaceutical Technology & Research*, *10*(3), 100–106.
- Berg, K. C. G., Eide, P. W., Eilertsen, I. A., Johannessen, B., Bruun, J., Danielsen, S. A., ... Lothe, R. A. (2017). Multi-omics of 34 colorectal cancer cell lines - a resource for biomedical studies. *Molecular Cancer*, *16*(116).
- Bernkop-Schnürch, A., & Steininger, S. (2000). Synthesis and characterisation of mucoadhesive thiolated polymers. *International Journal of Pharmaceutics*, *194*(2), 239–247.

- Bernkop-Schnürch, A., Hornof, M. D., Kast, C. E., & Langoth, N. (2002). Thiolated polymers: Stability of thiol moieties under different storage conditions. *Scientia Pharmaceutica*, *70*(4), 331–339.
- Beukema, M., Faas, M. M., & de Vos, P. (2020). The effects of different dietary fiber pectin structures on the gastrointestinal immune barrier: impact via gut microbiota and direct effects on immune cells. *Experimental & Molecular Medicine*, *52*, 1364–1376.
- Bhatt, A. P., Pellock, S. J., Biernat, K. A., Walton, W. G., Wallace, B. D., Creekmore, B. C., ... Redinbo, M. R. (2020). Targeted inhibition of gut bacterial β -glucuronidase activity enhances anticancer drug efficacy. *Proceedings of the National Academy of Sciences*, *201918095*.
- Bhattacharyya, G. S. (2010). Oral systemic therapy: Not all "win-win". *Indian Journal of Medical and Paediatric Oncology*, *31*(1), 1–3.
- Bigucci, F., Luppi, B., Cerchiara, T., Sorrenti, M., Bettinetti, G., Rodriguez, L., & Zecchi, V. (2008). Chitosan/pectin polyelectrolyte complexes: selection of suitable preparative conditions for colon-specific delivery of vancomycin. *European Journal of Pharmaceutical Sciences*, *35*(5), 435–441.
- Boddupalli, B. M., Mohammed, Z. N., Nath, R. A., & Banji, D. (2010). Mucoadhesive drug delivery system: An overview. *Journal of Advanced Pharmaceutical Technology & Research*, *1*(4), 381–387.
- Bose, A., Elyagoby, A., & Wong, T. W. (2014). Oral 5-fluorouracil colon-specific delivery through in vivo pellet coating for colon cancer and aberrant crypt foci treatment. *International Journal of Pharmaceutics*, *468*(1-2), 178–186.
- Bunz, F. (2008). Thymidylate synthase and 5-fluorouracil: a cautionary tale. *Cancer Biology & Therapy*, *7*(7), 995–996.
- Cao, Y., Gao, X., Zhang, W., Zhang, G., Nguyen, A. K., Liu, X., Jimenez, F., Cox, C. S., Jr, Townsend, C. M., Jr, & Ko, T. C. (2011). Dietary fiber enhances TGF- β signaling and growth inhibition in the gut. *American Journal of Physiology: Gastrointestinal and Liver Physiology*, *301*(1), G156–G164.
- Carulli, A. J., Keeley, T. M., Demitrack, E. S., Chung, J., Maillard, I., & Samuelson, L. C. (2015). Notch receptor regulation of intestinal stem cell homeostasis and crypt regeneration. *Developmental Biology*, *402*(1), 98–108.
- Cassidy, J., Douillard, J. Y., Twelves, C., McKendrick, J. J., Scheithauer, W., Bustová, I., Johnston, P. G., Lesniewski-Kmak, K., Jelic, S., Fountzilas, G., Coxon, F., Díaz-Rubio, E., Maughan, T. S., Malzyner, A., Bertetto, O., Beham, A., Figer, A., Dufour, P., Patel, K. K., Cowell, W., ... Garrison, L. P. (2006). Pharmacoeconomic analysis of adjuvant oral capecitabine vs intravenous 5-FU/LV in Dukes' C colon cancer: the X-ACT trial. *British Journal of Cancer*, *94*(8), 1122–1129.
- Cervantes, E., Martín, J. J., & Saadaoui, E. (2016). Updated Methods for Seed Shape Analysis. *Scientifica*, *2016*, 1–10.
- Chakravarti, B., Akhtar, T., Rai, B., Yadav, M., Akhtar Siddiqui, J., Dhar Dwivedi, S. K., Thakur, R., Singh, A. K., Singh, A. K., Kumar, H., Khan, K., Pal, S., Rath, S. K., Lal, J., Konwar, R., Trivedi, A. K., Datta, D., Mishra, D. P., Godbole, M. M., Sanyal, S., ... Kumar, A. (2014). Thioaryl naphthylmethanone oxime ether analogs as novel anticancer agents. *Journal of Medicinal Chemistry*, *57*(19), 8010–25.
- Chauhan, S. S., Shetty, A. B., Hatami, E., Chowdhury, P., & Yallapu, M. M. (2020). Pectin-Tannic Acid Nano-Complexes Promote the Delivery and Bioactivity of Drugs in Pancreatic Cancer Cells. *Pharmaceutics*, *12*(3), 285.
- Cheewatanakornkool, K., Niratisai, S., & Sriamornsak, P. (2015). Bioadhesiveness of thiolated pectin for buccal delivery of carbenoxolone sodium. *Asian Journal of Pharmaceutical Sciences*, *11*(1), 124–5.
- Cheewatanakornkool, K., Niratisai, S., Manchun, S., Dass, C. R., & Sriamornsak, P. (2017). Thiolated pectin–doxorubicin conjugates: Synthesis, characterization and anticancer activity studies. *Carbohydrate Polymers*, *174*, 493–506.
- Chen, K., Qiu, J.L., Zhang, Y., & Zhao, Y.W. (2003). Meta-analysis of risk factors for colorectal cancer. *World Journal of Gastroenterology*, *9*(7), 1598–1600.
- Chen, L., Hao, M., Yan, J., Sun, L., Tai, G., Cheng, H., & Zhao, Y. (2021). Citrus-derived DHCP inhibits mitochondrial complex II to enhance TRAIL sensitivity via ROS-induced DR5 upregulation. *Journal of Biological Chemistry*, *100515*.

- Cheng, H., Zhang, Z., Leng, J., Liu, D., Hao, M., Gao, X., Tai, G., & Zhou, Y. (2013). The inhibitory effects and mechanisms of rhamnogalacturonan I pectin from potato on HT-29 colon cancer cell proliferation and cell cycle progression. *International Journal of Food Sciences and Nutrition*, *64*(1), 36–43.
- Cheng, X., Zhang, X., Liu, P., Xia, L.-Y., Jiang, Y.-W., Gao, G., Wang, H.-Y., Li, Y.-H., Ma, N., Ran, H.-H., & Wu, F.-G. (2019). Sequential Treatment of Cell Cycle Regulator and Nanoradiosensitizer Achieves Enhanced Radiotherapeutic Outcome. *ACS Applied Biomaterials*, *2*, 2050-2059.
- Cho, H., Kim, J., Won, Y., Moon, K., & Seo, K. (2019). Inhibitory Effects of Pectinase-Treated *Prunus Mume* Fruit Concentrate on Colorectal Cancer Proliferation and Angiogenesis of Endothelial Cells. *Journal of Food Science*.
- Cho, Y., Turner, N. D., Davidson, L. A., Chapkin, R. S., Carroll, R. J., & Lupton, J. R. (2012). A chemoprotective fish oil/pectin diet enhances apoptosis via Bcl-2 promoter methylation in rat azoxymethane-induced carcinomas. *Experimental Biology and Medicine*, *237*(12), 1387–1393.
- Choi, H. S., Kim, K. H., Sohn, E., Park, J. D., Kim, B. O., Moon, E. Y., Rhee, D. K., & Pyo, S. (2008). Red ginseng acidic polysaccharide (RGAP) in combination with IFN-gamma results in enhanced macrophage function through activation of the NF-kappaB pathway. *Bioscience, Biotechnology, and Biochemistry*, *72*(7), 1817–1825.
- Chokradjaroen, C., Theeramunkong, S., Yui, H., Saito, N., & Rujiravanit, R. (2018). Cytotoxicity against cancer cells of chitosan oligosaccharides prepared from chitosan powder degraded by electrical discharge plasma. *Carbohydrate Polymers*, *201*, 20–30.
- Chotiko, A., & Sathivel, S. (2017). Releasing characteristics of anthocyanins extract in pectin–whey protein complex microcapsules coated with zein. *Journal of Food Science and Technology*, *54*(7), 2059–2066.
- Cui, S., & Chang, P. Y. (2016). Current understanding concerning intestinal stem cells. *World Journal of Gastroenterology*, *22*(31), 7099–7110.
- Dai, Z., Coker, O. O., Nakatsu, G., Wu, W. K. K., Zhao, L., Chen, Z., ... Yu, J. (2018). Multi-cohort analysis of colorectal cancer metagenome identified altered bacteria across populations and universal bacterial markers. *Microbiome*, *6*(1).
- Delphi, L., Sepehri, H., Khorramizadeh, M. R., & Mansoori, F. (2015). Pectic-Oligosaccharides from Apples Induce Apoptosis and Cell Cycle Arrest in MDA-MB-231 Cells, a Model of Human Breast Cancer. *Asian Pacific Journal of Cancer Prevention*, *16*(13), 5265–5271.
- Despres, J., Forano, E., Lepercq, P., Comtet-Marre, S., Jubelin, G., Yeoman, C. J., Miller, M. E., Fields, C. J., Terrapon, N., Le Bourvellec, C., Renard, C. M., Henrissat, B., White, B. A., & Mosoni, P. (2016). Unraveling the pectinolytic function of *Bacteroides xylanisolvens* using a RNA-seq approach and mutagenesis. *BMC Genomics*, *17*, 147.
- Do Nascimento, R. S., Pedrosa, L. de F., Diethelm, L. T. H., Souza, T., Shiga, T. M., & Fabi, J. P. (2020). The purification of pectin from commercial fruit flours results in a jaboticaba fraction that inhibits galectin-3 and colon cancer cell growth. *Food Research International*, *137*, 109747.
- Dutta, R. K., & Sahu, S. (2012). Development of diclofenac sodium loaded magnetic nanocarriers of pectin interacted with chitosan for targeted and sustained drug delivery. *Colloids and Surfaces B: Biointerfaces*, *97*, 19–26.
- Elyagoby, A., Layas, N., & Wong, T. W. (2013). Colon-Specific Delivery of 5-Fluorouracil from Zinc Pectinate Pellets through *in situ* Intracapsular Ethylcellulose–Pectin Plug Formation. *Journal of Pharmaceutical Sciences*, *102*(2), 604–616.
- Endo, K., Kohnoe, S., Tsujita, E., Watanabe, A., Nakashima, H., Baba, H., & Maehara, Y. (2005). Galectin-3 expression is a potent prognostic marker in colorectal cancer. *Anticancer Research*, *25*(4), 3117–3121.
- Entezar-Almahdi, E., Mohammadi-Samani, S., Tayebi, L., & Farjadian, F. (2020). Recent Advances in Designing 5-Fluorouracil Delivery Systems: A Stepping Stone in the Safe Treatment of Colorectal Cancer. *International Journal of Nanomedicine*, *15*, 5445–5458.

- Fichtner, M., Bozkurt, E., Salvucci, M., McCann, C., McAllister, K. A., Halang, L., ... Prehn, J. H. M. (2020). Molecular subtype-specific responses of colon cancer cells to the SMAC mimetic Birinapant. *Cell Death & Disease*, *11*(11).
- Fischer, B. E., Haring, U. K., Tribolet, R., & Sigel, H. (1979). Metal Ion/Buffer Interactions. Stability of Binary and Ternary Complexes Containing 2-Amino-2-(hydroxymethyl)-1,3-propanediol (Tris) and Adenosine 5'-Triphosphate (ATP). *European Journal of Biochemistry*, *94*(2), 523–530.
- Fleming, I., & Williams, D. (2019). *Spectroscopic Methods in Organic Chemistry*. Switzerland: Springer Nature, pp. 109-121.
- Fleming, M., Ravula, S., Tatishchev, S. F., & Wang, H. L. (2012). Colorectal carcinoma: Pathologic aspects. *Journal of Gastrointestinal Oncology*, *3*(3), 153–173.
- Föger, F., Hoyer, H., Kafedjiiski, K., Thaurer, M., & Bernkop-Schnürch, A. (2006). In vivo comparison of various polymeric and low molecular mass inhibitors of intestinal P-glycoprotein. *Biomaterials*, *27*(34), 5855–5860.
- Forman, H. J., Zhang, H., & Rinna, A. (2009). Glutathione: overview of its protective roles, measurement, and biosynthesis. *Molecular Aspects of Medicine*, *30*(1-2), 1–12.
- Fukunaga, T., Sasaki, M., Araki, Y., Okamoto, T., Yasuoka, T., Tsujikawa, T., Fujiyama, Y., & Bamba, T. (2003). Effects of the soluble fibre pectin on intestinal cell proliferation, fecal short chain fatty acid production and microbial population. *Digestion*, *67*(1-2), 42–49.
- Gao, X., Zhi, Y., Sun, L., Peng, X., Zhang, T., Xue, H., Tai, G., & Zhou, Y. (2013). The inhibitory effects of a rhamnogalacturonan I (RG-I) domain from ginseng pectin on galectin-3 and its structure-activity relationship. *The Journal of Biological Chemistry*, *288*(47), 33953–33965.
- Gibot, L., Chabaud, S., Bouhout, S., Bolduc, S., Auger, F. A., & Moulin, V. J. (2015). Anticancer properties of chitosan on human melanoma are cell line dependent. *International Journal of Biological Macromolecules*, *72*, 370–379.
- Grady, W.M. & Markowitz, S.D. (2014). The molecular pathogenesis of colorectal cancer and its potential application to colorectal cancer screening. *Digestive Diseases and Sciences*, *60*(3), 762–72.
- Greco, C., Vona, R., Cosimelli, M., Matarrese, P., Strafase, E., Scordati, P., Giannarelli, D., Casale, V., Assisi, D., Mottolese, M., Moles, A., & Malorni, W. (2004). Cell surface overexpression of galectin-3 and the presence of its ligand 90k in the blood plasma as determinants in colon neoplastic lesions. *Glycobiology*, *14*(9), 783–792.
- Gunning, A. P., Bongaerts, R. J. M., & Morris, V. J. (2009). Recognition of galactan components of pectin by galectin-3. *The FASEB Journal*, *23*(2), 415–424.
- Hamaguchi, T., Shimada, Y., Mizusawa, J., Kinugasa, Y., Kanemitsu, Y., Ohue, M., Fujii, S., Takiguchi, N., Yatsuoka, T., Takii, Y., Ojima, H., Masuko, H., Kubo, Y., Mishima, H., Yamaguchi, T., Bando, H., Sato, T., Kato, T., Nakamura, K., Fukuda, H., & Moriya, Y. (2018). Capecitabine versus S-1 as adjuvant chemotherapy for patients with stage III colorectal cancer (JCOG0910): an open-label, non-inferiority, randomised, phase 3, multicentre trial. *The Lancet. Gastroenterology & Hepatology*, *3*(1), 47–56.
- Hartig, S. M. (2013). Basic image analysis and manipulation in ImageJ. *Current Protocols in Molecular Biology*.
- He, W., Du, Q., Cao, D., Xiang, B., & Fan, L. (2008). Study on colon-specific pectin/ethylcellulose film-coated 5-fluorouracil pellets in rats. *International Journal of Pharmaceutics*, *348*(1-2), 35–45.
- Hibberd, A. A., Lyra, A., Ouwehand, A. C., Rolny, P., Lindegren, H., Cedgård, L., & Wettergren, Y. (2017). Intestinal microbiota is altered in patients with colon cancer and modified by probiotic intervention. *BMJ Open Gastroenterology*, *4*(1), e000145.
- Hintzen, F., Hauptstein, S., Perera, G., & Bernkop-Schnürch, A. (2013). Synthesis and in vitro characterization of entirely S-protected thiolated pectin for drug delivery. *European Journal of Pharmaceutics and Biopharmaceutics*, *85*(3), 1266–1273.
- Hossain, Z., & Takahashi, K. (2008). Induction of Permeability and Apoptosis in Colon Cancer Cell Line with Chitosan. *Journal of Food and Drug Analysis*, *16*(5), 1-8.

- Hosseini, G., Halvaei, S., Heidarian, Y., Dehghani-Ghobadi, Z., Hassani, M., Hosseini, H., Naderi, N., & Sheikh Hassani, S. (2019). Pectasol-C Modified Citrus Pectin targets Galectin-3-induced STAT3 activation and synergize paclitaxel cytotoxic effect on ovarian cancer spheroids. *Cancer Medicine*.
- Hsu, T.-C., Chen, H.-H., Yang, M.-C., Wang, H.-M., Chuang, J.-H., Jao, S.-W., ... Chen, L.-T. (2011). Pharmacoeconomic Analysis of Capecitabine versus 5-Fluorouracil/Leucovorin as Adjuvant Therapy for Stage III Colon Cancer in Taiwan. *Value in Health*, *14*(5), 647–651.
- Hua, S. (2019). Physiological and Pharmaceutical Considerations for Rectal Drug Formulations. *Frontiers in pharmacology*, *10*, 1196.
- Huang, X., & Brazel, C. S. (2001). On the importance and mechanisms of burst release in matrix-controlled drug delivery systems. *Journal of Controlled Release*, *73*(2-3), 121–136.
- Humblot, C., Murkovic, M., Rigottier-Gois, L., Bensaada, M., Bouclet, A., Andrieux, C., Anba, J., & Rabot, S. (2007). β -Glucuronidase in human intestinal microbiota is necessary for the colonic genotoxicity of the food-borne carcinogen 2-amino-3-methylimidazo[4,5-f]quinoline in rats. *Carcinogenesis*, *28*(11), 2419–2425.
- Ichikawa, M. (1979). The effect of hydrogen bonding on the bond lengths and angles in the carboxyl group. *Journal of Crystal and Molecular Structure*, *9*(2), 87–105.
- Ikeda, K., Yoshisue, K., Matsushima, E., Nagayama, S., Kobayashi, K., Tyson, C. A., Chiba, K., & Kawaguchi, Y. (2000). Bioactivation of tegafur to 5-fluorouracil is catalyzed by cytochrome P-450 2A6 in human liver microsomes *in vitro*. *Clinical Cancer Research*, *6*(11), 4409–4415.
- Ishisono, K., Mano, T., Yabe, T., & Kitaguchi, K. (2019). Dietary Fiber Pectin Ameliorates Experimental Colitis in a Neutral Sugar Side Chain-Dependent Manner. *Frontiers in Immunology*, *10*, 2979.
- Jabbour-Leung, N. A., Chen, X., Bui, T., Jiang, Y., Yang, D., Vijayaraghavan, S., McArthur, M. J., Hunt, K. K., & Keyomarsi, K. (2016). Sequential Combination Therapy of CDK Inhibition and Doxorubicin Is Synthetically Lethal in p53-Mutant Triple-Negative Breast Cancer. *Molecular Cancer Therapeutics*, *15*(4), 593–607.
- Jain, A., Gupta, Y., & Jain, S. K. (2007). Potential of calcium pectinate beads for target specific drug release to colon. *Journal of Drug Targeting*, *15*(4), 285–294.
- Jaiswal, M., & Lanjhiyana, S. K. (2018). Fabrication and Evaluations of Dual Crosslinked Mesalamine containing Pectin-Chitosan gel micro beads for controlled and targeted colon delivery. *Research Journal of Pharmacy and Technology*, *11*(11), 4797-4804.
- Johansson, M. E., Sjövall, H., & Hansson, G. C. (2013). The gastrointestinal mucus system in health and disease. *Nature Reviews Gastroenterology and Hepatology*, *10*(6), 352–361.
- Kadir, E. A., & Lim, V. (2020). Redox-Responsive Disulphide Bioadhesive Polymeric Nanoparticles for Colon-Targeted Drug Delivery. In: *Bioadhesives in Drug Delivery* (pp. 123-145).
- Kapoor, S., & Dharmesh, S.M. (2017). Pectic oligosaccharide from tomato exhibiting anticancer potential on a gastric cancer cell line: structure-function relationship. *Carbohydrate Polymers*, *160*, 52–61.
- Karki, S. S., Das, U., Umemura, N., Sakagami, H., Iwamoto, S., Kawase, M., ... Dimmock, J. R. (2016). 3,5-Bis(3-alkylaminomethyl-4-hydroxybenzylidene)-4-piperidones: A Novel Class of Potent Tumor-Selective Cytotoxins. *Journal of Medicinal Chemistry*, *59*(2), 763–769.
- Keizman, D., Frenkel, M.A., Peer, A., Rosenbaum, E., Mergel, D., Sarid, D., Neiman, V., Leibovitch, I., Sternberg, I. A., Boursi, B., Gottfried, M., Dresler, H., Eliaz, I. (2019). Effect of pectasol-c modified citrus pectin (P-MCP) treatment (tx) on PSA dynamics in non-metastatic biochemically relapsed prostate cancer (BRPC) patients (pts): Primary outcome analysis of a prospective phase II study. *Journal of Clinical Oncology*, *37*(15).
- Khotimchenko, M. (2020). Pectin polymers for colon-targeted antitumor drug delivery. *International Journal of Biological Macromolecules*, *S0141-8130(20)33147-0*.
- Khotimchenko, M.Y., Kolenchenko, E.A., & Khotimchenko, Y.S. (2008). Zinc-binding activity of different pectin compounds in aqueous solutions. *Journal of Colloid and Interface Science*, *323*(2), 216–222.
- Kim, A. D., Zhang, R., Han, X., Kang, K. A., Piao, M. J., Maeng, Y. H., Chang, W. Y., & Hyun, J. W. (2015). Involvement of glutathione and glutathione metabolizing enzymes in human colorectal cancer cell lines and tissues. *Molecular Medicine Reports*, *12*(3), 4314–4319.

- Kim, C. C., Kelly, W. J., Patchett, M. L., Tannock, G. W., Jordens, Z., Stoklosinski, H. M., Taylor, J. W., Sims, I. M., Bell, T. J., & Rosendale, D. I. (2017). *Monoglobus pectinilyticus* gen. nov., sp. nov., a pectinolytic bacterium isolated from human faeces. *International Journal of Systematic and Evolutionary Microbiology*, *67*(12), 4992–4998.
- Kolar, S. S., Barhoumi, R., Callaway, E. S., Fan, Y. Y., Wang, N., Lupton, J. R., & Chapkin, R. S. (2007). Synergy between docosahexaenoic acid and butyrate elicits p53-independent apoptosis via mitochondrial Ca²⁺ accumulation in colonocytes. *American Journal of Physiology: Gastrointestinal and Liver Physiology*, *293*(5), G935–G943.
- Kolar, S., Barhoumi, R., Jones, C. K., Wesley, J., Lupton, J. R., Fan, Y. Y., & Chapkin, R. S. (2011). Interactive effects of fatty acid and butyrate-induced mitochondrial Ca²⁺ loading and apoptosis in colonocytes. *Cancer*, *117*(23), 5294–5303.
- Kong, C. S., Bahn, Y. E., Kim, B. K., Lee, K. Y., & Park, K. Y. (2010). Antiproliferative effect of chitosan-added kimchi in HT-29 human colon carcinoma cells. *Journal of Medicinal Food*, *13*(1), 6–12.
- Koveitypour, Z., Panahi, F., Vakilian, M., Peymani, M., Seyed F. F., Nasr Esfahani, M. H., & Ghaedi, K. (2019). Signaling pathways involved in colorectal cancer progression. *Cell & Bioscience*, *9*(1).
- Kuipers, E. J., Grady, W. M., Lieberman, D., Seufferlein, T., Sung, J. J., Boelens, P. G., van de Velde, C. J., & Watanabe, T. (2015). Colorectal cancer. *Nature Reviews Disease Primers*, *1*, 15065.
- Kwakman, J. J., & Punt, C. J. (2016). Oral drugs in the treatment of metastatic colorectal cancer. *Expert Opinion on Pharmacotherapy*, *17*(10), 1351–1361.
- Labianca, R., Pancera, G., Aitini, E., Barni, S., Beretta, A., Beretta, G. D., Cesana, B., Comella, G., Cozzaglio, L., & Cristoni, M. (1991). Folinic acid + 5-fluorouracil (5-FU) versus equidose 5-FU in advanced colorectal cancer. Phase III study of 'GISCAD' (Italian Group for the Study of Digestive Tract Cancer). *Annals of Oncology*, *2*(9), 673–679.
- Lamberti, M., Porto, S., Marra, M., Zappavigna, S., Grimaldi, A., Feola, D., ... Pesce, D. (2012). 5-Fluorouracil induces apoptosis in rat cardiocytes through intracellular oxidative stress. *Journal of Experimental & Clinical Cancer Research*, *31*(1), 60.
- Leal, J., Smyth, H., & Ghosh, D. (2017). Physicochemical properties of mucus and their impact on transmucosal drug delivery. *International Journal of Pharmaceutics*, *532*(1), 555–572.
- Leclere, L., Fransolet, M., Cambier, P., El Bkassiny, S., Tikad, A., Dieu, M., Vincent, S. P., Van Cutsem, P., & Michiels, C. (2016). Identification of a cytotoxic molecule in heat-modified citrus pectin. *Carbohydrate Polymers*, *137*, 39–51.
- Leeming, E. R., Johnson, A. J., Spector, T. D., & Le Roy, C. I. (2019). Effect of Diet on the Gut Microbiota: Rethinking Intervention Duration. *Nutrients*, *11*(12), 2862.
- Legay, R., Massou S., Azéma, J., Martino, R., & Malet-Martino, M. (2014). Hydrolytic pathway of 5-fluorouracil in aqueous solutions for clinical use. *Journal of Pharmaceutical and Biomedical Analysis*, *98*, 446–462.
- León-González, A. J., López-Lázaro, M., Espartero, J. L., & Martín-Cordero, C. (2013). Cytotoxic activity of dihydrochalcones isolated from *Corema album* leaves against HT-29 colon cancer cells. *Natural Product Communications*, *8*(9), 1255–1256.
- Li, H., Wang, H., Wang, Z., Yan, H., Zhang, M., Liu, Y., & Cheng, M. (2018). Synthesis, antitumor activity evaluation and mechanistic study of novel hederacolchiside A₁ derivatives bearing an aryl triazole moiety. *Bioorganic & Medicinal Chemistry*, *26*(14), 4025–4033.
- Li, P., Wang, Y., Peng, Z., She, M. F., & Kong, L. (2010). Physicochemical property and morphology of 5-fluorouracil loaded chitosan nanoparticles. *2010 International Conference on Nanoscience and Nanotechnology*.
- Li, W., Hao, W., Xiaohua, Z., Yinchen, H., Wangwang, L., Gongming, Y., & Aimin, J. (2015). Pectin-chitosan complex: Preparation and application in colon-specific capsule. *International Journal of Agricultural and Biological Engineering*, *8*(4), 151-160.
- Lin, C.-C., & Fu, C.-H. (2009). Controlled release study of 5-fluorouracil-loaded chitosan/polyethylene glycol microparticles. *Drug Delivery*, *16*(5), 274–279.
- Linnekamp, J. F., Hooff, S., Prasetyanti, P. R., Kandimalla, R., Buikhuisen, J. Y., Fessler, E., Ramesh, P., Lee, K., Bochove, G., de Jong, J. H., Cameron, K., Leersum, R. V., Rodermond, H. M., Franitza, M.,

- Nürnberg, P., Mangiapane, L. R., Wang, X., Clevers, H., Vermeulen, L., Stassi, G., ... Medema, J. P. (2018). Consensus molecular subtypes of colorectal cancer are recapitulated in in vitro and in vivo models. *Cell Death and Differentiation*, *25*(3), 616–633.
- Liu, L., Fishman, M. L., Hicks, K. B., Kende, M., & Ruthel, G. (2006). Pectin/Zein Beads for Potential Colon-Specific Drug Delivery: Synthesis and *in Vitro* Evaluation. *Drug Delivery*, *13*(6), 417–423.
- Liu, L., Li, Y. H., Niu, Y. B., Sun, Y., Guo, Z. J., Li, Q., Li, C., Feng, J., Cao, S. S., & Mei, Q. B. (2010). An apple oligogalactan prevents against inflammation and carcinogenesis by targeting LPS/TLR4/NF- κ B pathway in a mouse model of colitis-associated colon cancer. *Carcinogenesis*, *31*(10), 1822–32.
- Liu, W., Zhang, R., Shu, R., Yu, J., Li, H., Long, H., ... Wu, Q. (2020). Study of the Relationship between Microbiome and Colorectal Cancer Susceptibility Using 16SrRNA Sequencing. *BioMed Research International*, *2020*, 7828392.
- Longley, D. B., Harkin, D. P., & Johnston, P. G. (2003). 5-Fluorouracil: mechanisms of action and clinical strategies. *Nature Reviews Cancer*, *3*(5), 330–338.
- Lopez-Siles, M., Khan, T. M., Duncan, S. H., Harmsen, H. J., Garcia-Gil, L. J., & Flint, H. J. (2012). Cultured representatives of two major phylogroups of human colonic *Faecalibacterium prausnitzii* can utilize pectin, uronic acids, and host-derived substrates for growth. *Applied and Environmental Microbiology*, *78*(2), 420–428.
- Maciel, V. B. V., Yoshida, C. M. P., & Franco, T. T. (2015). Chitosan/pectin polyelectrolyte complex as a pH indicator. *Carbohydrate Polymers*, *132*, 537–545.
- Mahajan, H.S., Tyagi, V.K., Patil, R.R., & Dusunge, S.B. (2013). Thiolated xyloglucan: Synthesis, characterization and evaluation as mucoadhesive *in situ* gelling agent. *Carbohydrate Polymers*, *91*(2), 618–625.
- Majzoob, S., Atyabi, F., Dorkoosh, F., Kafedjiiski, K., Loretz, B., & Bernkop-Schnürch, A. (2006). Pectin-cysteine conjugate: synthesis and in-vitro evaluation of its potential for drug delivery. *The Journal of Pharmacy and Pharmacology*, *58*(12), 1601–1610.
- Martens, E. C., Lowe, E. C., Chiang, H., Pudlo, N. A., Wu, M., McNulty, N. P., Abbott, D. W., Henrissat, B., Gilbert, H. J., Bolam, D. N., & Gordon, J. I. (2011). Recognition and degradation of plant cell wall polysaccharides by two human gut symbionts. *PLoS Biology*, *9*(12), e1001221.
- Martínez-Maqueda, D., Miralles, B., & Recio, I. (2015). HT29 Cell Line. In: Verhoeckx K, Cotter P, López-Expósito I, et al., editors. *The Impact of Food Bioactives on Health: in vitro and ex vivo models* [Internet]. Cham (CH): Springer. Chapter 11. [Retrieved 7 March 2021]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK500137/>
- Martins, A. L. L., de Oliveira, A. C., do Nascimento, C. M. O. L., Silva, L. A. D., Gaeti, M. P. N., Lima, E. M., & Marreto, R. N. (2017). Mucoadhesive Properties of Thiolated Pectin-Based Pellets Prepared by Extrusion-Spheronization Technique. *Journal of Pharmaceutical Sciences*, *106*(5), 1363–1370.
- Masuda, S., Azuma, K., Kurozumi, S., Kiyose, M., Osaki, T., Tsuka, T., Itoh, N., Imagawa, T., Minami, S., Sato, K., & Okamoto, Y. (2014). Anti-tumor properties of orally administered glucosamine and N-acetyl-D-glucosamine oligomers in a mouse model. *Carbohydrate Polymers*, *111*, 783–787.
- Maxwell, E. G. (2014). *Effects of Modified Bioactive Pectins on Colon Cancer Cells in vitro*. [Doctoral Dissertation, University of East Anglia, Norwich, England]. Retrieved from <https://ethos.bl.uk/OrderDetails.do?uin=uk.bl.ethos.637553>
- Maxwell, E. G., Colquhoun, I. J., Chau, H. K., Hotchkiss, A. T., Waldron, K. W., Morris, V. J., & Belshaw, N. J. (2015). Rhamnogalacturonan I containing homogalacturonan inhibits colon cancer cell proliferation by decreasing ICAM1 expression. *Carbohydrate Polymers*, *132*, 546–553.
- Meldrum, O. W., Yakubov, G. E., Bonilla, M. R., Deshmukh, O., McGuckin, M. A., & Gidley, M. J. (2018). Mucin gel assembly is controlled by a collective action of non-mucin proteins, disulfide bridges, Ca²⁺-mediated links, and hydrogen bonding. *Scientific Reports*, *8*(1), 5802.
- Miller, M.C., Zheng, Y., Zhou, Y., Tai, G., & Mayo, K.H. (2019). Galectin-3 binds selectively to the terminal, non-reducing end of β (1→4)-galactans, with overall affinity increasing with chain length. *Glycobiology*.

- Miura, K., Kinouchi, M., Ishida, K., Fujibuchi, W., Naitoh, T., Ogawa, H., Ando, T., Yazaki, N., Watanabe, K., Haneda, S., Shibata, C., & Sasaki, I. (2010). 5-FU metabolism in cancer and orally-administrable 5-fu drugs. *Cancers*, 2(3), 1717–1730.
- Müller, M. F., Ibrahim, A. E., & Arends, M. J. (2016). Molecular Pathological classification of colorectal cancer. *Virchows Archiv*, 469(2), 125–134.
- Naghibalhossaini, F., Shefaghat, M., Mansouri, A., Jaber, H., Tatar, M., & Eftekhari, E. (2017). The impact of thymidylate synthase and methylenetetrahydrofolate reductase genotypes on sensitivity to 5-fluorouracil treatment in colorectal cancer cells. *Acta Medica Iranica*, 55(12), 751-8.
- Nam, K. S., Kim, M. K., & Shon, Y. H. (2007). Inhibition of proinflammatory cytokine-induced invasiveness of HT-29 cells by chitosan oligosaccharide. *Journal of Microbiology and Biotechnology*, 17(12), 2042–2045.
- Nawaz, A., & Wong, T. W. (2020). Chitosan as Anticancer Compound and Nanoparticulate Matrix for Cancer Therapeutics. *Encyclopedia of Marine Biotechnology*, 1737–1752.
- Noordhuis, P., Holwerda, U., Van der Wilt, C. L., Van Groeningen, C. J., Smid, K., Meijer, S., Pinedo, H. M., & Peters, G. J. (2004). 5-Fluorouracil incorporation into RNA and DNA in relation to thymidylate synthase inhibition of human colorectal cancers. *Annals of Oncology*, 15(7), 1025–1032.
- Ogut, F. O., Mu, T. H., Sun, H., & Zhang, M. (2018). Ultrasonic Modified Sweet Potato Pectin Induces Apoptosis like Cell Death in Colon Cancer (HT-29) Cell Line. *Nutrition and Cancer*, 70(1), 136–145.
- Ohwada, S., Sato, Y., Izumi, M., Kashiwabara, K., Ogawa, T., Hamada, K., Kawate, S., & Nakamura, S. (2006). Preoperative tegafur suppositories for resectable rectal cancer: phase II trial. *Diseases of the Colon and Rectum*, 49(10), 1602–1610.
- Oka, N., Nakahara, S., Takenaka, Y., Fukumori, T., Hogan, V., Kanayama, H.O., Yanagawa, T., & Raz, A. (2005). Galectin-3 inhibits tumor necrosis factor-related apoptosis-inducing ligand-induced apoptosis by activating Akt in human bladder carcinoma cells. *Cancer Research*, 65, 7546–7553.
- Okabayashi, K., Hasegawa, H., Watanabe, M., Ohishi, T., Hisa, A., & Kitagawa, Y. (2012). Usefulness of the Preoperative Administration of Tegafur Suppositories as Alternative Adjuvant Chemotherapy for Patients with Resectable Stage II or III Colorectal Cancer: A KODK4 Multicenter Randomized Control Trial. *Oncology*, 83(1), 16–23.
- Pandey, S., Mishra, A., Raval, P., Patel, H., Gupta, A., & Shah, D. (2013). Chitosan-pectin polyelectrolyte complex as a carrier for colon targeted drug delivery. *Journal of Young Pharmacists*, 5(4), 160–166.
- Pardini, B., Kumar, R., Naccarati, A., Novotny, J., Prasad, R. B., Forst, A., Hemminki, K., Vodicka, P., & Lorenzo Bermejo, J. (2011). 5-Fluorouracil-based chemotherapy for colorectal cancer and MTHFR/MTRR genotypes. *British Journal of Clinical Pharmacology*, 72(1), 162–163.
- Park, J. K., Chung, M. J., Choi, H. N., & Park, Y. I. (2011). Effects of the molecular weight and the degree of deacetylation of chitosan oligosaccharides on antitumor activity. *International Journal of Molecular Sciences*, 12(1), 266–277.
- Patsos, H. A., Hicks, D. J., Dobson, R. R., Greenhough, A., Woodman, N., Lane, J. D., Williams, A. C., & Paraskeva, C. (2005). The endogenous cannabinoid, anandamide, induces cell death in colorectal carcinoma cells: a possible role for cyclooxygenase 2. *Gut*, 54(12), 1741–1750.
- Pedrosa, L. F., Lopes, R. G., & Fabi, J. P. (2020). The acid and neutral fractions of pectins isolated from ripe and overripe papayas differentially affect galectin-3 inhibition and colon cancer cell growth. *International Journal of Biological Macromolecules*, 164, 2681–2690.
- Perera, G., Hombach, J., & Bernkop-Schnürch, A. (2010). Hydrophobic thiolation of pectin with 4-aminothiophenol: synthesis and in vitro characterization. *AAPS PharmSciTech*, 11(1), 174–180.
- Pizzorno, G., Sun, Z., & Handschumacher, R.E. (1995). Aberrant cell cycle inhibition pattern in human colon carcinoma cell lines after exposure to 5-fluorouracil. *Biochemical Pharmacology*, 49(4), 553-7
- Prado, S. B. R. do, Ferreira, G. F., Harazono, Y., Shiga, T. M., Raz, A., Carpita, N. C., & Fabi, J. P. (2017). Ripening-induced chemical modifications of papaya pectin inhibit cancer cell proliferation. *Scientific Reports*, 7(1).
- Puga, A. M., Lima, A. C., Mano, J. F., Concheiro, A., & Alvarez-Lorenzo, C. (2013). Pectin-coated chitosan microgels crosslinked on superhydrophobic surfaces for 5-fluorouracil encapsulation. *Carbohydrate Polymers*, 98(1), 331–340.

- Quan, H., Zhu, F., Han, X., Xu, Z., Zhao, Y., & Miao, Z. (2009). Mechanism of anti-angiogenic activities of chitooligosaccharides may be through inhibiting heparanase activity. *Medical Hypotheses*, 73(2), 205–206.
- Rabeneck, L., Horton, S., Zauber, A. G., & Earle, C. (2015). Colorectal Cancer. In: Gelband H, Jha P, Sankaranarayanan R, *et al.*, editors. *Cancer: Disease Control Priorities, Third Edition (Volume 3)* [Internet]. Washington DC: The International Bank for Reconstruction and Development/The World Bank. Chapter 6. [Retrieved 23 December 2020]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK343633/>
- Rai, N. K., Mathur, S., Singh, S. K., Tiwari, M., Singh, V. K., Haque, R., Tiwari, S., & Kumar Sharma, L. (2020). Differential regulation of mitochondrial complex I and oxidative stress based on metastatic potential of colorectal cancer cells. *Oncology Letters*, 20(6), 313.
- Raj, A. A. S., Rubila, S., Jayabalan, R., & Ranganathan, T. V. (2012). A Review on Pectin: Chemistry due to General Properties of Pectin and its Pharmaceutical Uses. *Open Access Scientific Reports*, 1(12).
- Rajendran, D. T., Subramaniyan, B., & Ganeshan, M. (2017). Role of Notch signaling in colorectal cancer. In: *Role of Transcription Factors in Gastrointestinal Malignancies*. Singapore: Springer, pp. 307-314.
- Ramachandran, C., Wilk, B. J., Hotchkiss, A., Chau, H., Eliaz, I., & Melnick, S. J. (2011). Activation of human T-helper/inducer cell, T-cytotoxic cell, B-cell, and natural killer (NK)-cells and induction of natural killer cell activity against K562 chronic myeloid leukemia cells with modified citrus pectin. *BMC Complementary and Alternative Medicine*, 11, 59.
- Ramteke, K. H., & Nath, L. (2014). Formulation, evaluation and optimization of pectin-bora rice beads for colon targeted drug delivery system. *Advanced Pharmaceutical Bulletin*, 4(2), 167–177.
- Rinninella, E., Raoul, P., Cintoni, M., Franceschi, F., Miggiano, G., Gasbarrini, A., & Mele, M. C. (2019). What is the Healthy Gut Microbiota Composition? A Changing Ecosystem across Age, Environment, Diet, and Diseases. *Microorganisms*, 7(1), 14.
- Rutman, R. J., Cantarow, A., & Paschkis, K. E. (1954). The catabolism of uracil in vivo and in vitro. *Journal of Biological Chemistry*, 210, 321-329.
- Sacco, P., Pedroso-Santana, S., Kumar, Y., Joly, N., Martin, P., & Bocchetta, P. (2021). Iontropic Gelation of Chitosan Flat Structures and Potential Applications. *Molecules (Basel, Switzerland)*, 26(3), 660.
- Sahankumari, P., Gamage, B. D., & Malavige, G. N. (2019). Association of the gut microbiota with colorectal cancer in a South Asian cohort of patients. *BioRxiv*.
- Sahlberg, S. H., Spiegelberg, D., Glimelius, B., Stenerlöw, B., & Nestor, M. (2014). Evaluation of cancer stem cell markers CD133, CD44, CD24: association with AKT isoforms and radiation resistance in colon cancer cells. *PLoS one*, 9(4), e94621.
- Samuel, A. J., Kulkarni, M., & Tambe, R. (2010). Thiomers: forms, features, and formulations. *Journal of Chemical and Pharmaceutical Research*, 2(6), 316-323.
- Satelli, A., Rao, P., Gupta, P., Lockman, P., Srivenugopal, K., & Rao, U. (2008). Varied expression and localization of multiple galectins in different cancer cell lines. *Oncology Reports*.
- Sayuti, M. & Nauva. (2019). Kanker Kolorektal. *Averrous: Jurnal Kedokteran dan Kesehatan Malikussaleh*, 5(2), 76-88.
- Schmoll, H. J. (2003). Dihydropyrimidine dehydrogenase inhibition as a strategy for the oral administration of 5-fluorouracil: utility in the treatment of advanced colorectal cancer. *Anti-cancer drugs*, 14(9), 695–702.
- Senapati, S., Mahanta, A. K., Kumar, S., & Maiti, P. (2018). Controlled drug delivery vehicles for cancer treatment and their performance. *Signal Transduction and Targeted Therapy*, 3, 7.
- Shafabakhsh, R., Yousefi, B., Asemi, Z., Nikfar, B., Mansournia, M. A., & Hallajzadeh, J. (2020). Chitosan: a compound for drug delivery system in gastric cancer-a review. *Carbohydrate Polymers*, 116403.
- Shah, M. S., Schwartz, S. L., Zhao, C., Davidson, L. A., Zhou, B., Lupton, J. R., Ivanov, I., & Chapkin, R. S. (2011). Integrated microRNA and mRNA expression profiling in a rat colon carcinogenesis model: effect of a chemo-protective diet. *Physiological Genomics*, 43(10), 640–654.

- Sharma, R. & Ahuja, M. (2011). Thiolated pectin: Synthesis, Characterization and Evaluation as a Mucoadhesive Polymer. *Carbohydrate Polymers*, 85(3), 658–663.
- Shen, L., Luo, H.-S., Sun, J., & Zhao, L. (2011). Leptin decreases the sensitivity of human colon cancer cell HT-29 to 5-fluorouracil. *African Journal of Pharmacy and Pharmacology*, 5(7), 979-984.
- Sheng, Q., Du, H., Cheng, X., Cheng, X., Tang, Y., Pan, L., Wang, Q., & Lin, J. (2019). Characteristics of fecal gut microbiota in patients with colorectal cancer at different stages and different sites. *Oncology Letters*, 18(5), 4834–4844.
- Sigel, H., Scheller, K. H., & Prijs, B. (1982). Metal ion/buffer interactions. Stability of alkali and alkaline earth ion complexes with triethanolamine (tea), 2-amino-2(hydroxymethyl)-1,3-propanediol (tris) and 2-[bis(2-hydroxyethyl)-amino] 2(hydroxymethyl)-1,3-propanediol (Bistris) in aqueous and mixed solvents. *Inorganica Chimica Acta*, 66, 147–155.
- Sonkar, S. K., Ganeshan, N., Mathur, M., & Lanjhiyana, S. K. (2021). Colon Targeting of 5-fluorouracil Loaded Dual Cross-linked Multiparticulate System: *In vitro* and *in vivo* Characterizations. *Asian Journal of Pharmaceutics*, 15(1), 82-93.
- Sriamornsak, P. (2011). Application of Pectin in Oral Drug Delivery. *Expert Opinion on Drug Delivery*, 8(8), 1009–1023.
- Stankevicius, V., Kunigenas, L., Stankunas, E., Kuodyte, K., Strainiene, E., Cicenias, J., Samalavicius, N. E., & Suziedelis, K. (2017). The expression of cancer stem cell markers in human colorectal carcinoma cells in a microenvironment dependent manner. *Biochemical and Biophysical Research Communications*, 484(4), 726–733.
- Subudhi, M. B., Jain, A., Jain, A., Hurkat, P., Shilpi, S., Gulbake, A., & Jain, S. K. (2015). Eudragit S100 Coated Citrus Pectin Nanoparticles for Colon Targeting of 5-Fluorouracil. *Materials (Basel, Switzerland)*, 8(3), 832–849.
- Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, I., Jemal, A., & Bray, F. (2021). Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal For clinicians*, 10.3322/caac.21660.
- Suzuki, O., Hirsch, B., Abe, M., Dürkop, H., & Stein, H. (2011). Galectin-1-mediated cell death is increased by CD30-induced signaling in anaplastic large cell lymphoma cells but not in Hodgkin lymphoma cells. *Laboratory Investigation*, 92(2), 191–199.
- Tao, L., Jin, L., Dechun, L., Hongqiang, Y., Changhua, K., & Guijun, L. (2017). Galectin-3 Expression in Colorectal Cancer and its Correlation with Clinical Pathological Characteristics and Prognosis. *Open Medicine (Warsaw, Poland)*, 12, 226–230.
- Thirawong, N., Nunthanid, J., Puttipipatkachorn, S., & Sriamornsak, P. (2007). Mucoadhesive properties of various pectins on gastrointestinal mucosa: an *in vitro* evaluation using texture analyzer. *European Journal of Pharmaceutics and Biopharmaceutics*, 67(1), 132–140.
- Tiğli Aydın, R. S., & Pulat, M. (2012). 5-Fluorouracil Encapsulated Chitosan Nanoparticles for pH-Stimulated Drug Delivery: Evaluation of Controlled Release Kinetics. *Journal of Nanomaterials*, 2012, 1–10.
- Traverso, N., Ricciarelli, R., Nitti, M., Marengo, B., Furfaro, A. L., Pronzato, M. A., Marinari, U. M., & Domenicotti, C. (2013). Role of glutathione in cancer progression and chemoresistance. *Oxidative Medicine and Cellular Longevity*, 2013, 972913.
- van Beek, M., Roukens, M., Jacobs, W., Timmer-Bonte, J., & Kramers, C. (2018). Real-World Adverse Effects of Capecitabine Toxicity in an Elderly Population. *Drugs-Real World Outcomes*, 5(3), 161-7.
- van den Mooter, G., Samyn, C. & Kinget, R. (1995). In Vivo Evaluation of a Colon-Specific Drug Delivery System: An Absorption Study of Theophylline from Capsules Coated with Azo Polymers in Rats. *Pharmaceutical Research*, 12, 244–247.
- van Hoogdalem, E., de Boer, A. G., & Breimer, D. D. (1991). Pharmacokinetics of rectal drug administration, Part I. General considerations and clinical applications of centrally acting drugs. *Clinical Pharmacokinetics*, 21(1), 11–26.
- Varghese, V., Magnani, L., Harada-Shoji, N., Mauri, F., Szydło, R. M., Yao, S., ... Kenny, L. M. (2019). FOXM1 modulates 5-FU resistance in colorectal cancer through regulating TYMS expression. *Scientific Reports*, 9(1).

- Vijayaraghavalu, S., Dermawan, J. K., Cheriya, V., & Labhasetwar, V. (2013). Highly synergistic effect of sequential treatment with epigenetic and anticancer drugs to overcome drug resistance in breast cancer cells is mediated via activation of p21 gene expression leading to G2/M cycle arrest. *Molecular Pharmaceutics*, *10*(1), 337–352.
- Vodenkova, S., Buchler, T., Cervena, K., Veskrnova, V., Vodicka, P., & Vymetalkova, V. (2019). 5-fluorouracil and other fluoropyrimidines in colorectal cancer: Past, present and future. *Pharmacology and Therapeutics*, *107447*.
- Vogus, D. R., Pusuluri, A., Chen, R., & Mitragotri, S. (2018). Schedule dependent synergy of gemcitabine and doxorubicin: Improvement of in vitro efficacy and lack of in vitro-in vivo correlation. *Bioengineering & Translational Medicine*, *3*(1), 49–57.
- Wang, H., Yang, B., & Sun, H. Y. (2017). Pectin-Chitosan Polyelectrolyte Complex Nanoparticles for Encapsulation and Controlled Release of Nisin. *American Journal of Polymer Science and Technology*, *3*(5), 82-88.
- Wang, H., Sun, H. Y., & He, J. Y. (2017). Formation of Polyelectrolyte Complex Colloid Particles between Chitosan and Pectin with Different Degree of Esterification. *IOP Conference Series: Materials Science and Engineering*, *275*, 012012.
- Wang, M., Vogel, I., & Kalthoff, H. (2003). Correlation between metastatic potential and variants from colorectal tumor cell line HT-29. *World Journal of Gastroenterology*, *9*(11), 2627–2631.
- Wang, S., Li, P., Lu, S. M., & Ling, Z. Q. (2016). Chemoprevention of Low-Molecular-Weight Citrus Pectin (LCP) in Gastrointestinal Cancer Cells. *International Journal of Biological Sciences*, *12*(6), 746-756.
- Wang, T. M. M., Lau, W. M., & Khutoryanskiy, V. V. (2018). Chitosan and Its Derivatives for Application in Mucoadhesive Drug Delivery Systems. *Polymers*, *10*(3), 267.
- Welsh, S. J., Hobbs, S., & Aherne, G. W. (2003). Expression of uracil DNA glycosylase (UDG) does not affect cellular sensitivity to thymidylate synthase (TS) inhibition. *European Journal of Cancer*, *39*(3), 378–387.
- Wielnińska, J., Nowacki, A., & Liberek, B. (2019). 5-Fluorouracil – Complete Insight into Its Neutral and Ionised Forms. *Molecules (Basel, Switzerland)*, *24*(20), 3683.
- Wikiera, A., Grabacka, M., Byczynski, L., Stodolak, B., & Mika, M. (2021). Enzymatically Extracted Apple Pectin Possesses Antioxidant and Antitumor Activity. *Molecules*, *2021*(26), 1434.
- Wong, S.H., & Yu, J. (2019). Gut microbiota in colorectal cancer: mechanisms of action and clinical applications. *Nature Reviews Gastroenterology & Hepatology*, *16*, 690–704.
- Xiao, L., Ge, X., Yang, L., Chen, X., Xu, Q., Rui, X., & Li, W. (2020). Anticancer potential of exopolysaccharide from *Lactobacillus helveticus* MB2-1 on human colon cancer HT-29 cell via apoptosis induction. *Food & Function*.
- Xu, Y., & Pasche, B. (2007). TGF-beta signaling alterations and susceptibility to colorectal cancer. *Human Molecular Genetics*, *16 Spec No 1*(SPEC), R14–R20.
- Yamakita, E., & Nakashima, S. (2018). Water Retention of Calcium-Containing Pectin Studied by Quartz Crystal Microbalance and Infrared Spectroscopy with a Humidity Control System. *Journal of Agricultural and Food Chemistry*, *66*(35), 9344–9352.
- Yang, Y., Yang, L., Zhou, L., & Tang, S. (2021). A Critical Review of the Effect of Dietary Fiber Intake on the Prevention of Colorectal Cancer in Eastern Asian Countries. *Journal of Healthcare Engineering*, *2021*, 6680698.
- Yeung, T. M., Gandhi, S. C., Wilding, J. L., Muschel, R., & Bodmer, W. F. (2010). Cancer stem cells from colorectal cancer-derived cell lines. *Proceedings of the National Academy of Sciences of the United States of America*, *107*(8), 3722–3727.
- Yoshida, M., Ishiguro, M., Ikejiri, K., Mochizuki, I., Nakamoto, Y., Kinugasa, Y., Takagane, A., Endo, T., Shinozaki, H., Takii, Y., Mochizuki, H., Kotake, K., Kameoka, S., Takahashi, K., Watanabe, T., Watanabe, M., Boku, N., Tomita, N., Nakatani, E., Sugihara, K., ... ACTS-CC study group (2014). S-1 as adjuvant chemotherapy for stage III colon cancer: a randomized phase III study (ACTS-CC trial). *Annals of Oncology*, *25*(9), 1743–1749.

- Yu, F., Finley, R. L., Jr, Raz, A., & Kim, H. R. (2002). Galectin-3 translocates to the perinuclear membranes and inhibits cytochrome c release from the mitochondria. A role for synexin in galectin-3 translocation. *The Journal of Biological Chemistry*, 277(18), 15819–15827.
- Zaitseva, O., Khudyakov, A., Sergushkina, M., Solomina, O., & Polezhaeva, T. (2020). Pectins as a universal medicine. *Fitoterapia*, 146, 104676.
- Zamorano-León, J. J., Ballesteros, S., de Las Heras, N., Alvarez-Sala, L., de la Serna-Soto, M., Zekri-Nechar, K., ... López-Farré, A. J. (2019). Effect of pectin on the expression of proteins associated with mitochondrial biogenesis and cell senescence in HT29-human colorectal adenocarcinoma cells. *Preventive Nutrition and Food Science*, 24(2), 187–196.
- Zeuner, B., Thomsen, T. B., Stringer, M. A., Krogh, K., Meyer, A. S., & Holck, J. (2020). Comparative Characterization of *Aspergillus* Pectin Lyases by Discriminative Substrate Degradation Profiling. *Frontiers in Bioengineering and Biotechnology*, 8, 873.
- Zhao, W., Huang, X.-X., Yu, L.-H., Liu, Q.-B., Li, L.-Z., Sun, Q., & Song, S.-J. (2014). Tomensides A–D, new antiproliferative phenylpropanoid sucrose esters from *Prunus tomentosa* leaves. *Bioorganic & Medicinal Chemistry Letters*, 24(11), 2459–2462.
- Zhao, Z. Y., Liang, L., Fan, X., Yu, Z., Hotchkiss, A. T., Wilk, B. J., & Eliaz, I. (2008). The role of modified citrus pectin as an effective chelator of lead in children hospitalized with toxic lead levels. *Alternative Therapies in Health and Medicine*, 14(4), 34–38.