# CANCER MECHANISM, MOLECULAR TARGETS AND CHEMOTHERAPEUTIC PHYTOCHEMICALS; A REVIEW

## Sana Riaz<sup>\*</sup>, Naaz Abbas, Sania Mazhar, Ishrat Perveen, Saira Ashfaq, Ramsha Essa, Yasar Saleem, Quratulain Syed and Syed Hussain Abidi

Pakistan Council of Scientific and Industrial Research (PCSIR) Laboratories Complex Lahore

Corresponding Author Email: <a href="mailto:sanariazpk@gmail.com">sanariazpk@gmail.com</a>

#### Abstract

The uncontrolled multiplication of cells prompts cell aggregation, primary change and hereditary hazards at last outcome in the arrangement of dangerous cells. Present day clinical indications for malignant growth the executives have a few unfriendly impacts including restricted bioavailability, non-particularity, harmful impact on different cells or tissue. These treatments include chemotherapy, immunotherapy, medical procedure of cancers and radiotherapy and immature microorganism treatment. By investigating Chemotheapeutic capability of restorative plants look for new, novel medication applicants can be investigated from the a huge number of year's effective customary therapeutic framework checked by the current day, high level present day research procedures and innovation. This would be useful for feasible, conservable, normal asset that can bring about cost administration, drug creation upgrade and medication arrangement or overabundance to the enduring populace.

Keywords: Cancer mechanism, Medicinal plants, Anticancer, Phytochemicals

### **INTRODUCTION**

Current chemotherapeutic choices are restricted to chemotherapy, radiotherapy, medical procedure, DNA-intuitive specialists and chemotherapeutic medications are either cytostatic or cytotoxic which profoundly successful against wide reach malignant growths in blend with different medications (Arya *et al.*, 1992). Chemotherapeutic medications are produced for restraint of uncontrolled development of unusual growth cells the objective of these medications is overwhelmingly acceptance of apoptosis, otherwise called customized cell passing, is the most massively explored subject in present day cell

#### *The Journal of Microbiology and Molecular Genetics (JMMG) Vol. 3, No. 3 (2022), pp. 21-30*

science (Khatak *et al.*, 2018). Aftereffects at last lessen the blood creation and lead to aggravation, immunosuppression and sensory system problems. Malignant growth is the most destroying sickness of hundred years with the most noteworthy pace of bleakness and mortality (Kligerman *et al.*, 2019). The uncontrolled multiplication of cells prompts cell amassing, primary change and hereditary dangers eventually bring about the development of threatening cells (Lim and Leprivier, 2019). The pace of occurrence for malignant growth is higher in evolved nations than non-industrial nations (Ullah *et al.*, 2019) in any case, the pace of mortality is more noteworthy in emerging nations because of compromised medical services offices, oppressed anticipation and excessively expensive therapies choices (Figure 1).

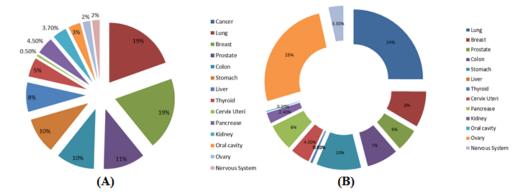


Figure 1: (A) Organ specific cancer cases reported worldwide till 2018 (B) Organ specific cancer deaths reported worldwide (Data source globocan 2018).

### Cancer mechanism and molecular targets

Malignant growth is made by unusual cell expansion which drives the peculiar mass development that might happen in a body cells or tissue. There are proof for the pathway that telomerase is responsible for limitless engendering which typically abbreviated with time in customary cells are communicated at altogether in deified changed disease cells. Moreover, obstruction in bad criticism component ensures proceeded with expansion a model is a change in Ras transforms Ras GTPase likewise the movement which hinders the natural negative input circle. Additionally, carcinoma cells likewise produce earlier fiery signs encompassing internal environment.

### **Programmed Cellular Apoptosis**

The process of apoptosis is crucial for normal cell death of radiation-damaged cells as well as for the effectiveness of anticancer drugs used in repetitive cycles. This knowledge is crucial for developing medications that specifically target the apoptotic pathways and the desired features (Khan *et al.*, 2016).

At different levels, these cycles might be involved with drug-induced disease cell death. There are two main paths for apoptosis, and two of them, the inherent and extraneous pathways, finally trigger the normal process (Figure 2) (Khan *et al.*, 2020). Caspases, which are activated by Poly (ADP-ribose) polymerase to cause DNA fracture, are the final goal in the two processes (PARP).

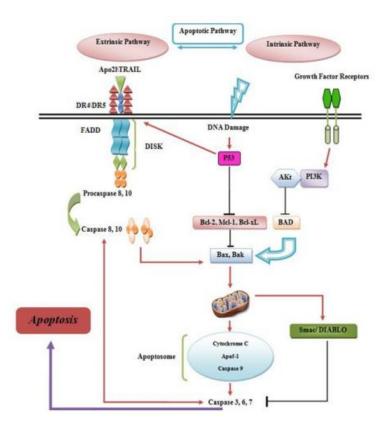


Figure 2: Schematic representation of comparison of intrinsic (driven by mitrocondria) and extrinsic pathway (Mollazadeh *et al.*, 2017).

## **Intrinsic and Extrinsic Pathway**

The natural route inside mitochondria utilises many proteins there (Khan *et al.*, 2020) because of the specific signals elicited, film to promote apoptosis. Internal cell conditions, inherited weakness, DNA damage and cellular stress increased cytosolic calcium centralizations, trigger the typical route process. These lead to increased cytochrome c porousness and a reduction in the ability of the BCl2 protein family. This increases cytochrome c delivery, has been observed that drugs can cause cancer cells to undergo apoptosis. PARP inhibitors, extended being unique objective for late illness treatmentconsidered as interesting target. While inside endoplasmic reticulum instruments outstandingly

less revelations played the critical occupation in controlling played by p53 (Delgado-Vargas *et al.*, 2018).

## Phytochemiclas with Chemptherapeutic Effect

The authentic scenery of productive anticancer medicine exposure from supportive plants offers sound assistance for extra disclosure of novel chemotherapeutic or chemopreventive phyto-compounds. Phytochemical eliminates through sensible systems can yield various valuable typical things which advance prosperity without coincidental impacts. A couple of auxiliaries of paclitaxel are under clinical primers at the public Threatening development Foundation for mix treatment against ovarian, bladder, lung and chest infection (Iqbal *et al.*, 2017). Vinca alkaloids bind to tubulin limiting site which upsets microtubules capacity that prompts cellcycle catch (Rohilla and Garg, 2014). Camptothecin, screened as a reasonable amedicine from *Camptotheca acuminata* for anticancer potential has a spot with the family, Nyssaceae. Auxiliaries pneumonic carcinoma the farmer for as expert arranged as topoisomerase I, inhibitor by hailing wellsprings and preventing sickness (Kumawat *et al.*, 2012).

## **Molecular Targets**

The term threatening development neutralization suggests control of dangerous development at a fundamental stage or to hinder the event of the ailment, it could in like manner consolidate toning down, or exchanging disorder (Milchteim *et al.*, 2018). The elective procedure for the treatment of sickness furthermore have huge degree (Moore *et al.*, 2015). This is a specific goal arranged approach and consolidates disease causing specialist processing, free radical looking through activity, detoxification and DNA fix procedure and antipromotion or antiprogression.

## CONCLUSION

Taking everything into account, configuration advance investigation for atomic association instrument and translations of pharmacokinetics and pharmacodynamics preceding clinical preliminaries. This inherent intricacy of novel normal item drug improvement and disclosure to battle disease is a profoundly incorporated and interdisciplinary methodology. Also, biochemical profiling from bioactive phytochemicals can prompt green anticancer objective determined drug up-and-comers from lab to advertise.

## REFERENCES

Akbar, M., Javaid, A., Ahmed, E., Javed, T. and Clary, J. 2014. Holadysenterine, a natural herbicidal constituent from *Drechslera australiensis* for management of Rumex dentatus. *Journal of Agricultural and Food Chemistry*, **62**: 368-372.

Al-Dhaheri, W., Hassouna, I. and Karam, S. M. 2018. Genetic polymorphisms and protein expression of P53 and BRCA1 in preneoplastic and neoplastic rat mammary glands. *Oncology Reports*, **39**: 2193-2200.

Ansar, M., Ashfaq, U. A., Sarwar, M. T., Javed, T., Rehman, S., Hassan, S. and Riazuddin, S. 2011. Inhibition of full length hepatitis C virus particles of 1a genotype through small interference RNA. *Virology Journal*, **8**: 203.

Arya, S., Toky, O., Harris, S. and Harris, P. 1992. Tecomella undulata (Rohira): a valuable tree of the thar desert. *International Tree Crops Journal*, **7**:141-147.

Bahadur, S., Khan, M. S., Shah, M., Shuaib, M., Ahmad, M., Zafar, M., Begum, N., Gul, S., Ashfaq, S. and Mujahid, I. 2018. Traditional usage of medicinal plants among the local communities of Peshawar valley, Pakistan. *Acta Ecologica Sinica*.

Baldim, J. L., Rosa, W., Santos, M. F. C., Chagas-Paula, D. A., Lago, J. H. G. and Soares, M. G. 2017. Homoisoflavonoids from Caesalpinia spp.: A Closer Look at Chemical and Biological Aspects. *Flavonoids: From Biosynthesis to Human Health*:97.

Boskovic, I., Đukić, D. A., Maskovic, P., Mandić, L. and Perovic, S. 2018. Phytochemical composition and antimicrobial, antioxidant and cytotoxic activities of *Anchusa officinalis* L. extracts. *Biologia*, **73**: 1035-1041.

Burger, T. M. 2016. In vitro P-glycoprotein activity of alkaloid-enriched fractions from Solanum aculeastrum and its synergistic potential with doxorubicin. University of Pretoria.

Carnes, S., O'Brien, S., Szewczak, A., Tremeau-Cayel, L., Rowe, W. F., McCord, B. and Lurie, I. S. 2017. Comparison of ultra high performance supercritical fluid chromatography, ultra high performance liquid chromatography, and gas chromatography for the separation of synthetic cathinones. *Journal of Separation science*, **40**: 3545-3556.

Chen, X.-J., Ni, L., Bao, M.-F., Wang, L. and Cai, X.-H. 2017. Abietane diterpenoids from Cephalotaxus lanceolata. *Natural product research*, **31**: 2473-2478.

Contreras-+, M. d. M., Bribi, N., Gómez-Caravaca, A. M., Gálvez, J. and Segura-Carretero, A. 2017. Alkaloids Profiling of Fumaria capreolata by Analytical Platforms Based on the Hyphenation of Gas Chromatography and Liquid Chromatography with Quadrupole-Time-of-Flight Mass Spectrometry. *International journal of analytical chemistry*, **2017**.

Delgado-Vargas, F., Sicairos-Medina, L. Y., Luna-Mandujan, A. G., López-Angulo, G., Salazar-Salas, N. Y., Vega-García, M. O., Heredia, J. B. and López-Valenzuela, J. Á. 2018. Phenolic profiles, antioxidant and antimutagenic activities of Solanum lycopersicum var. cerasiforme accessions from Mexico. *CyTA-Journal of Food*, **16**: 715-722.

Di Sotto, A., Di Giacomo, S., Amatore, D., Locatelli, M., Vitalone, A., Toniolo, C., Rotino, G. L., Lo Scalzo, R., Palamara, A. T. and Marcocci, M. E. 2018. A polyphenol rich extract from Solanum melongena L. DR2 peel exhibits antioxidant properties and anti-Herpes Simplex Virus Type 1 activity in vitro. *Molecules*, **23**: 2066.

Elshamy, A. I., Farrag, A.-R. H., Mohamed, S. H., Ali, N. A., Mohamed, T. A., Menshawy, M. M., Zaglool, A. W., Efferth, T. and Hegazy, M.-E. F. 2019. Gastroprotective effects of ursolic acid isolated from *Ochrosia elliptica* on ethanol-induced gastric ulcer in rats. *Medicinal Chemistry Research*, 1-13.

Fan, J.-Y., Chen, H.-B., Zhu, L., Chen, H.-L., Zhao, Z.-Z. and Yi, T. 2015. *Saussurea medusa*, source of the medicinal herb snow lotus: a review of its botany, phytochemistry, pharmacology and toxicology. *Phytochemistry Reviews*, **14**: 353-366.

Frenk, A. and Sivakumar, G. 2017. Transcriptome Analysis of Colchicine Producing Plant Species: *Gloriosa superba* and *Colchicum autumnale*.

Haake, A., Nguyen, K., Friedman, L., Chakkamparambil, B. and Grossberg, G. T. 2020. An update on the utility and safety of cholinesterase inhibitors for the treatment of Alzheimer's disease. *Expert Opinion On Drug Safety*, **19**: 147-157.

Higashi, Y., Ikeda, Y. and Fujii, Y. 2016. Combination of pretreatments with acetic acid and sodium methoxide for efficient digoxin preparation from digitalis glycosides in digitalis lanata leaves. *Pharmacology & Pharmacy*, **7**: 200.

Hoadley, K. A., Yau, C., Hinoue, T., Wolf, D. M., Lazar, A. J., Drill, E., Shen, R., Taylor, A. M., Cherniack, A. D. and Thorsson, V. 2018. Cell-of-origin patterns dominate the molecular classification of 10,000 tumors from 33 types of cancer. *Cell*, **173**: 291-304.

Iqbal, J., Abbasi, B. A., Mahmood, T., Kanwal, S., Ali, B., Shah, S. A. and Khalil, A. T. 2017. Plantderived anticancer agents: A green anticancer approach. *Asian Pacific Journal of Tropical Biomedicine*, **7**: 1129-1150.

Javed, T., Riaz, S., Uzair, M., Mustafa, G., Mohyuddin, A. and Ahmad, B. 2016. Biological activity of *Terminalia arjuna* on human pathogenic microorganisms. *Pakistan Journal of Pharmaceuteucical Research*, **2**: 23-27.

Jiang, G., Liu, J., Ren, B., Zhang, L., Owusu, L., Liu, L., Zhang, J., Tang, Y. and Li, W. 2017. Antitumor and chemosensitization effects of Cryptotanshinone extracted from Salvia miltiorrhiza Bge. on ovarian cancer cells in vitro. *Journal of ethnopharmacology*, **205**:33-40.

Khan, T., Ali, M., Khan, A., Nisar, P., Jan, S. A., Afridi, S. and Shinwari, Z. K. 2020. Anticancer Plants: A review of the active phytochemicals, applications in animal models, and regulatory aspects. *Biomolecules*, **10**: 47.

Khan, T., Abbasi, B. H., Khan, M. A. and Shinwari, Z. K. 2016. Differential effects of thidiazuron on production of anticancer phenolic compounds in callus cultures of *Fagonia indica*. *Applied Biochemistry and Biotechnology*, **179**: 46-58.

Khatak, S., Sharma, A. and Saini, R. 2018. Comparative analysis of plant growth regulators on bud break in Prosopsis and Tecomella for sustainable agriculture in arid and semi-arid regions of India. *An International Peer Reviewed Open Access Journal For Rapid Publication*: 208.

Kligerman, M. P., Sethi, R. K., Kozin, E. D., Gray, S. T. and Shrime, M. G. 2019. Morbidity and mortality among patients with head and neck cancer in the emergency department: A national perspective. *Head & Neck*, **41**: 1007-1015.

Kumar, P., Jaiswal, V., Pal, T., Singh, J. and Chauhan, R. S. 2017. Comparative whole-transcriptome analysis in *Podophyllum* species identifies key transcription factors contributing to biosynthesis of podophyllotoxin in *P. hexandrum*. *Protoplasma*, **254**: 217-228.

Kumawat, R., Sharma, S. and Kumar, S. 2012. An overview for various aspects of multifaceted, health care tecomella undulata seem plant. *Acta Poloniae Pharmaceutica*, **69**: 993-996.

Lim, J. K. and Leprivier, G. 2019. The impact of oncogenic RAS on redox balance and implications for cancer development. *Cell Death & Disease*, **10**: 1-9.

Mahmood, S., Faraz, R., Yousaf, A., Asif, H. and Badar, F. 2015. Cancer Registry and Clinical Data Management (CRCDM)—Shaukat Khanum Memorial Cancer Hospital and Research Center (SKMCH & RC)—Report Based on Cancer Cases Registered at SKMCH & RC from December 1994–December 2014 and in 2014. *Released June*.

Milchteim, M., Katske, F. A. and Rajfer, J. 2018. Methods and compositions for extending the efficacy of phosphodiesterase inhibitors for treating erectile dysfunction, and compositions for inhibiting the onset and slowing the progression of erectile dysfunction. Google Patents.

Mollazadeh, H., Afshari, A. R. and Hosseinzadeh, H. 2017. Review on the potential therapeutic roles of *Nigella sativa* in the treatment of patients with cancer: Involvement of apoptosis:-black cumin and cancer. *Journal of Pharmacopuncture*, **20**: 158.

Moore, Z., Chakrabarti, G., Luo, X., Ali, A., Hu, Z., Fattah, F., Vemireddy, R., DeBerardinis, R., Brekken, R. and Boothman, D. 2015. NAMPT inhibition sensitizes pancreatic adenocarcinoma cells to tumor-selective, PAR-independent metabolic catastrophe and cell death induced by  $\beta$ -lapachone. *Cell Death & Disease*, **6** :e1599-e1599.

Moroh, J.-L. A., Fleury, Y., Coulibaly, A., Labia, R. and Leguérinel, I. 2019. Chemo-diversity of antibacterial anthraquinones from the roots of *Morinda morindoides*. *The Natural Products Journal*, **9**: 256-261.

Qiao, H., Cui, Z., Yang, S., Ji, D., Wang, Y., Yang, Y., Han, X., Fan, Q., Qin, A. and Wang, T. 2017. Targeting osteocytes to attenuate early breast cancer bone metastasis by theranostic upconversion nanoparticles with responsive plumbagin release. *ACS Nano*, **11**: 7259-7273.

Rehman, S., Ashfaq, U. A. and Javed, T. 2011. Antiviral drugs against hepatitis C virus. *Genetic Vaccines and Therapy*, **9**: 11.

Rohilla, R. and Garg, M. 2014. Phytochemistry and pharmacology of *Tecomella undulata*. *International Journal of Green Pharmacy (IJGP)*, **8**.

Rupnik-Cigoj, M., Jež-Krebelj, A., Castellarin, S. D., Trošt, K., Sivilotti, P. and Pompe-Novak, M. 2018. Grapevine fanleaf virus affects grape (*Vitis vinifera*) berry anthocyanin content via the transcriptional regulation of anthocyanin biosynthetic genes. *Functional Plant Biology*, **45**: 771-782.

Satdive, R., Shinde, A. N., Singh, S., Kamble, S., Singh, S., Malpathak, N. and Fulzele, D. P. 2015. Aggregate cell suspension cultures of *Psoralea corylifolia* improved phytoestrogens production. *Biotechnology and Bioprocess Engineering*, **20**: 373-379.

Shi, J., Huo, R., Li, N., Li, H., Zhai, T., Li, H., Shen, B., Ye, J., Fu, R. and Di, W. 2019. CYR61, a potential biomarker of tumor inflammatory response in epithelial ovarian cancer microenvironment of tumor progress. *BMC Cancer*, **19**:1-8.

Ullah, S., Ali, M., Din, M., Afridi, S., Bashir, S. and Shinwari, Z. K. 2019. Bioinspired synthesis of nanoparticles and their biomedical potential: the Pakistan experience. *Proceedings of the Pakistan Academy of Sciences: B. Life and Environmental Sciences*, **56**: 37–47.

Vieites, F. M., Araújo, G. M., Souza, C. S., Névoa, M. L., Vargas Júnior, J. G. d., Nunes, R. V. and Arruda, N. V. M. D. 2015. Minerals balance and performance of broilers at 21 days of age fed diet containing *Solanum malacoxylon. Revista Brasileira de Saúde e Produção Animal*, **16**: 535-543.

Wang, T., Li, P., Sun, Y., Song, X., Li, H., Qin, L., Zhou, J., Huang, Q. and Lei, F. 2020. Camptothecin-imprinted polymer microspheres with rosin-based cross-linker for separation of camptothecin from *Camptotheca acuminata* fruit. *Separation and Purification Technology*, **234**: 116085.

Zhang, S., Cheng, F., Yang, L., Zeng, J., Han, F., Yu, X., Zhu, Y., Zhong, G. and He, J. 2019. Chemical constituents from *Glehnia littoralis* and their chemotaxonomic significance. *Natural Product Research*, 1-6.

*The Journal of Microbiology and Molecular Genetics (JMMG) Vol. 3, No. 3 (2022), pp. 21-30* 

Zhen, Y. and Yu, Y. 2018. Proteomic analysis of the downstream signaling network of PARP1. *Biochemistry*, **57**: 429-440.