EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES

http://www.ejbps.com

ISSN 2349-8870
Volume: 9
Issue: 6
173-179
Year: 2022

A QUICK OVERVIEW OF CURCUMIN, AN HERBAL MEDICINE, IS USED IN CHEMOTHERAPY IN CARCINOMA

Sneha N. Wankhede*[1], Dr. Jagdish R. Baheti[2], Dr. Mangesh D. Godbole[2], Minakshi S.Warghane[2]

Kamla Nehru College of Pharmacy Buttibori Nagpur.441108.

***Corresponding Author: Sneha N. Wankhede**

Kamla Nehru College of Pharmacy Buttibori Nagpur.441108.

Article Received on 07/04/2022 **Article Revised on 27/04/2022** **Article Accepted on 17/05/2022**

ABSTRACT

Cancer is the second leading cause of death and a major public health problem. Cancer mortality remains high. Curcumin is a naturally occurring phytochemical obtained from the dried roots and rhizomes of turmeric (Curcuma longa). Shown to interfere with cell signalling pathways. Apoptosis, proliferation, angiogenesis and inflammation Most of the analogues showed excellent antitumor activity in many cell lines. Curcumin deficiency is due to low solubility, poor absorption, rapid metabolism, and elimination. Recent research has shown that several compounds and techniques to increase the bioavailability of curcumin mixed with excipients, encapsulated in a carrier, and nano formed with different bioactive. Structural analogues of curcumin, have increased efficacy and bioavailability. In this review, comprehensive literature on the anti-tumor activity of curcumin through combination therapy, structural modification, synthesis analogues and novel delivery systems is presented. Many challenges relate to curcumin as an adjuvant chemotherapeutic agent and emphasize further clinical studies.

KEYWORDS: Curcumin, Nano-curcumin, Herbal drug, Bioavailability, Anticancer agents, Cellular pathway.

INTRODUCTION

Chinese herbs derived from botanical extracts are increasingly being used to treat a variety of illnesses. There is growing interest in the pharmacological evaluation of various plants used in traditional Indian medicine. Indian Materia Medica contains 2000 therapeutically important natural products, 400 of which are of mineral and animal origin and the rest of which are of plant origin. There are about 1250 medicinal plants in India used to prescribe remedies. Plants and other natural products can affect human health. The effects of herbal extracts and isolates have been tested in pharmacological models. There is always a need for new and effective treatments.[1]

Synthetic work offers relatively few improvements over the prototype drug. There is often a need for a new prototype, and new models to design a potential agent. Natural products that provide such samples are economical with low toxicity. The long-term use of synthetic substances is very dangerous; therefore, attention should be paid to a drug with an antitumor activity that is intrinsically not or less toxic than synthetic drugs. Naturopathic medicine has been established and widely recognized as safe and effective in such ailments. Naturopathic Medicine provides a system in which the active ingredient of a crude drug of natural origin can be formulated and manufactured in a dosage form approved by the allergy medicine system.[2]

Cancers are uncontrollable abnormal cells in the body. Cancer develops when the body's normal control mechanisms stop working. The old cells do not die and develop into new abnormal cells. These cells can form a mass of tissue called a tumor. Cancers such as leukemia do not form tumors. Cancer can occur anywhere in the body. For women, breast cancer is one of the most common diseases. In men, it is prostate cancer. Lung cancer and colorectal cancer affect both men and women.

It is the deadliest disease with millions of people suffering from cancer or dying from its harmful effects. More than a hundred different types of cancer. It is one of the most difficult diseases for anyone trying to discover promising cancer drugs[3].The discovery and development of anticancer agents is a focus of many pharmaceutical companies and other organizations, such as the National Cancer Institute (NCI). Development of cancer therapy due to incomplete understanding of tumor formation. Cancer pharmacology has facilitated the development of a targeted drug designed to inhibit a molecule involved in cancer growth and metastasis.

Pre-Clinical Study

A. Preliminary in-vitro screening: In-vitro cell culture models are used to evaluate the antitumorigenic activity of new drug candidates. More than 10000 drugs are tested in in-vitro models yearly to investigate the extent and specificity of anti-cancerous activity.

B. pre-clinical in-vivo testing
Evaluation of drug toxicity and efficacy in animals.

CLINICAL STUDY
Toxicity was tested in volunteers to determine the maximally tolerated dose in phase 1 clinical trials to evaluate the efficacy and confirm dosing, phase 2 studies were conducted in patients with the selected tumor type, followed by large-scale phase 3 studies. development of the 10,000 drugs screened, typically only 100 are tested in preclinical studies, 510 enter clinical trials, and only 1 or 2 are ultimately approved by the NDA. favourable as a marketed drug for treatment. The average time from synthesizing a new compound to receiving marketing authorization is about 9 to 12 years, with an average cost of $0.5 to $2 billion depending on the disease.[4,5]

TYPES OF CANCER (CARCINOMA)
A] Carcinomas begin in the skin or tissues that line the internal organs.
B] Sarcomas develop in the bone, cartilage, fat, muscle, or other connective tissues.
C] Leukaemia begins in the blood and bone marrow.
D] Lymphomas start in the immune system.
E] Central nervous system cancer formed in the brain and spinal cord

Treatment depends on the type of cancer, the stage, whether cancer has spread, and the goal of treatment is to kill cancer cells while reducing damage to nearby normal cells Using technology makes this possible.

TREATMENTS
Surgery: directly removing the tumor
Chemotherapy: using chemicals to kill cancer cells
Radiation therapy: using X-rays to kill cancer cells.[4,5]

Cancer is the second leading cause of global mortality rates. In general, the proportion of cancer has increased; In the United States alone, about 1,665,540 people with cancer and 585,720 people died of this disease in 2014.[6] Therefore, cancer is a serious problem that affects the health of all species society People. Unfortunately, it is a diverse tissue disease and this variety is a major challenge for its specific diagnosis, then the effectiveness of treatment.[7,8] In men, the highest rate of cancer occurs in the prostate, lungs and bronchial, colon and rectal, and bladder, respectively. In women, the highest rate of cancer is in the chest, lungs and bronchial, colon and rectum, uterus, and thyroid, respectively. These data indicate that prostate cancer and breast cancer are major parts of cancer in men and women, respectively.[9] For children, the highest rate of cancer is blood cancer and concerned cancer in turn to cerebral and lymph nodes.[10,11]

Cancer occurs through a series of consecutive mutations in genes so that these mutations change cell functions. Chemical compounds have a clear role in the formation of genetic mutations and cancer cells. In addition, smoking is associated with certain cancer-causing chemical compounds that lead to lung cancer.[12] Interestingly, environmental chemicals with carcinogenic properties directly or indirectly affect the cytoplasm and nucleus of cells and lead to genetic disorders and genetic mutations.[13,14,15,16] Viruses, bacteria, and radiation are other factors in carcinogenesis, accounting for 7% of all cancers.[17] In general, cancer disrupts cellular relationships and causes important genes to malfunction. This disruption affects the cell cycle and leads to abnormal proliferation.[18,19] Proto oncogenes are responsible for cell division and growth under normal conditions, but become cancerous when mutated, which is the most dangerous to cell survival.[20]

In addition, the absence of tumor suppressor genes triggers uncontrolled cell division.[21] Typically, repair genes lead to proteins and enzymes with substitution properties and more than 30 types of repair proteins have been discovered.[21,22] Removal of uracil from DNA bypasses DNA damage and prevents primary DNA damage caused by UV rays, which is essentially the function of repair genes for successful DNA repair.[23]

Epigenetics is a dynamic situation in the study of cell fate and epigenetic modifications such as DNA methylation, histone modifications, and nucleosome location, which play important roles in cancer formation letters.[24,25] Cancer cells are characterized by a significant decrease in DNA methylation. (Approximately 5-6% reduction in total 5-methyl cytosine)[26] The overall reduction of monoacetylated H4K16 accounts for the majority of histone changes in cancer cells,[27] All families of chromatin-modifying proteins have been implicated in cancer, although in most cases the underlying molecular mechanisms of their function remain unknown.[28]

Nanotechnology in Cancer Therapies
Nanomedicine and nano-delivery systems are a relatively new but rapidly evolving science in which nano-sized materials are used as diagnostic tools or to deliver therapeutic agents to therapeutic sites. specifically targeted in a controlled manner. Nanotechnology offers many advantages in the treatment of chronic human diseases through targeted and targeted delivery of specific drugs. Recently, there are several prominent applications of nanomedicine (chemotherapy agent, biological agent, immunotherapeutic agent etc. In the treatment of various diseases, the present review presents a summary.

Update on recent advances in nanomedicine and deliver nano-based drugs through an in-depth examination of the discovery and application of nanomaterials to improve the efficacy of both new and old drugs (Ex. Natural products) and selective diagnosis using disease marker molecules, their clinical applications are also discussed. In addition, we have included information about trends and prospects in the field of nanomedicine. Since ancient

times, people have widely used natural herbal products as medicines for various diseases. Modern medicine is mainly derived from herbs based on traditional knowledge and practices. Almost 25% of the major pharmaceutical compounds and their derivatives today are obtained from natural resources.[29,30]

Natural compounds with different molecular backgrounds have a facility to explore new drugs. A recent trend in detecting natural drug products is the design point of lead molecules to reduce the synthesis and mimic their partners' chemistry,[31] Natural products have remarkable characteristics such as special chemical diversity, chemical and biological nature with macromolecular specificity, and less toxicity. They make fines favourable for detecting new drugs.[32]

In addition, calculation studies have contributed to considering molecular drug interactions and developing subsequent generation medication envisions such as drugs and drugs. Although there are many advantages, pharmaceutical companies do not want to invest more in drugs and drug discovery systems,[33] and explore libraries of chemical compounds available to explore different types. New drugs. However, natural compounds are currently being predicted to treat some major diseases, including cancer, diabetes, cardiovascular, inflammation, and microbiology. This is mainly because natural drugs have unique advantages, such as lower toxicity and side effects, low cost, and good therapeutic potential. However, concerns regarding the biocompatibility and toxicity of natural compounds present a greater challenge to their medicinal use. As a result, many natural compounds fail to pass clinical trials because of these problems.[34,35,36]

The use of large materials in drug delivery poses major challenges, including in vivo instability, low bioavailability and low solubility, and poor absorption in the body targeted administration issues, supplement effectiveness, and possible side effects. effects of drugs. Therefore, the use of novel drug delivery systems to target drugs to specific parts of the body may be an option that can address these important problems and delivered with great success.[37,38]

CURCUMIN

Curcumin is a yellow chemical obtained from plants of the species *Curcuma longa.* It is a member of the ginger family, *Zingiberaceae.* Chemically, curcumin is a "substance" belonging to the group of curcuminoids, which are phenolic pigments that give turmeric its yellow colour.

In 1815, Vogel and Pierre Joseph Pelletier reported for the first time the isolation of a "yellow colorant" from the rhizome of turmeric called curcumin. Turns out it was a mixture of resin and turmeric oil. Curcumin has historically been used in Ayurvedic medicine, but its potential medicinal properties are still unproven as therapy when used orally.

Curcumin is the largest component of Rhizomes *Curcuma Longa L* and up to extract from a Curcuma tree in a pure crystalline form for the first time in Curcumin 1870 and its derivatives have received big attention. Over the past two decades, they interested due to their biological nature. For example, antioxidant and anti-inflammatory activities.

Fig. I: Curcumin obtained from *Curcuma Longa* belonging to a family *Zingiberaceae.*

These properties are attributed to the main elements of the Curcumin Structure. As a result, many scientific works have exploded largely on the structure of curcumin (SAR). To try to improve its physical and biological properties. Because the importance of cancer is the cause of death and permanent tasks for anti-cancer agents more effective and less toxic anti-cancer operations. The main mechanisms of curcumin action are exposed to its unique anti-cancer activity including the touch of apoptosis and the inhibition of tumor

proliferation and encroachment by removing a variety of signal channels Cells Some studies have reported anti-cancer curcumin, lung cancer, head, and neck.

Cell carcinoma, prostate cancer, and brain tumors show the ability to target some cancer cell lines. Although all the benefits have been mentioned above, the curcumin applications are limited due to low water solubility causing low oral bioavailability and low chemical stability. The absence of obstacles is a low curcumin absorption. Conventions, lead to the availability of low curcumin inside the cytoplasm. To overcome these obstacles and improve the overall activity of curcuminian cancer, some structural changes have been proposed to improve toxicity for specific cancer cells and increase the ability to Use and stability.[39,40]

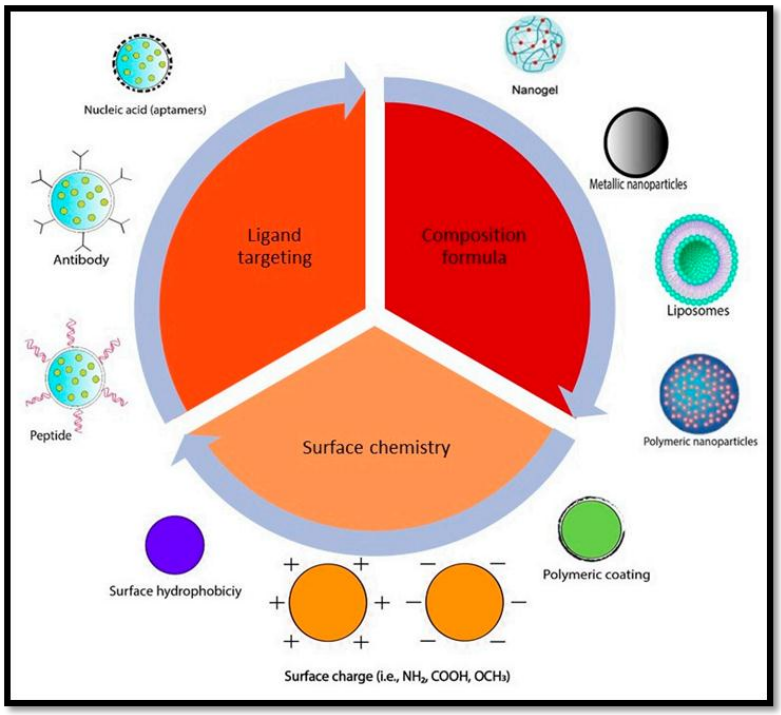

Fig. II. Examples of current nanoparticle design strategies used to improve targeting.

Different Types of Curcumin Delivery Systems Used In Cancer Therapy

Different curcumin delivery systems have been constructed using different nanotechnology to improve curcumin's properties and targeting capabilities. To rationally design nano formulas, several factors must be taken into account to increase the efficacy and improve the cellular targeting of anticancer agents. These factors include the size and shape of the nanoparticles, and the properties and target ligands of the nanoparticles. The most commonly used curcumin delivery systems are presented as follows.[41]

A. Polymeric Nanoparticles

PLGA poly (lactic-co-glycolic acid) and natural polymers such as fibroin silk and chitosan have become widely used in drug delivery. PLGA curcumin nanoparticles have been increased compared with unprocessed curcumin to be distributed Combined with piperine an alkaloid compound, however, combination administration of curcumin/piperine enhanced curcumin's activity by inhibiting hepatic and intestinal inactivation.[42]

B. Liposomes

The liposomal formulation improves the treatment of drug-resistant tumors and reduces toxicity. A liposome consists of a phospholipid bilayer and an aqueous core, making it the ideal medium for encapsulating hydrophobic and hydrophilic compounds. Several liposomal preparations have been used to encapsulate curcumin. PLGA or poly (caprolactone) (PCL) nanoparticles, liposomal and self-assembled formulations of curcumin should be of highest priority for cancer therapeutic applications due to their biocompatibility.[42]

C. Nanogels

Nanogels have attracted considerable attention over the past decade as a promising drug delivery system, with only a handful of studies, have investigated the delivery of curcumin nano-gel in cancer therapy. Natural polymers, chitosan, chitin, and alginate are the most studied for the preparation of nanogels for drug delivery.[43]

D. Nanophytosomes

Phytosomes are a lipid-based vesicular delivery system used to encapsulate plant-based drugs and nutritional compounds. The phytosome delivery system could reduce problems related to the solubility and

bioavailability of polyphenolic compounds, making them applicable in new drug development. Phytosomes can improve the bioavailability of polyphenolic compounds in the gastrointestinal tract and reduce the dose. Polyphenolic compounds are more effective treatments for cancer and other diseases, making Phytosome technology an excellent encapsulation platform for use in future nano-formulation of nutraceuticals.[44]

ANTICANCER ACTIVITY OF CURCUMIN

One of the main causes of cancer is an imbalance between cells and cell deaths. When cells die due to the absence of apoptotic signals, uncontrollable cells occur, leading to different types of cancer. Apoptotic signals are created through two main channels: internal paths and external paths. The intracellular route works by stimulating the mitochondrial membrane to inhibit the expression of anti-trace proteins. Curcumin disrupts the balance of mitochondrial membrane potential, leading to inhibition of protein increases. The extrinsic apoptotic pathway works by increasing death receptors (SDRs) on cells and activating tumor necrosis factor (TNF)-related apoptosis.

Curcumin also contributes to this pathway by regulating the expression of death receptors DR 4 and DR 5. In vitro studies have shown the remarkable ability of curcumin and its derivatives to inhibit induce apoptosis in different cell lines by inhibiting or down-regulating intracellular transcription factors. These factors include NFκB, activator protein 1 (AP1), cyclooxygenase II (COX2), nitric oxide synthase, matrix metalloproteinase9 (MMP9), and STAT3. Recent work has identified a novel antitumor mechanism for curcumin by reducing glucose uptake and lactate production (Warburg effect) in cancer cells through upregulation of pyruvate kinase M2 (PKM2). Inhibition of PKM2 was achieved by knocking out the mammalian target of hypoxia-inducible factor 1α (TORHIF1α) for mammals. Several studies have investigated the ability of curcumin and its derivatives to suppress several different types of cancer by interacting with different molecular targets.[45]

Table I: Changes to the pharmacological activity of curcumin derivatives compared to curcumin.

Sr. No	Curcumin Derivative	Chemical Modification	Activities	References
1	Dimethyl curcumin (ASC-J9)	Methyl groups substitution on R2 and R4	Enhanced activity toward prostate and breast cancer	[40]
2	Vanadium, gallium, and indium complexes	Metal complexation by the β-diketones	Enhanced cytotoxic activity	[41]
3	Tetrahydro-curcumin (THC)	Hydrogenated diketone moiety	Enhanced antioxidant activity but the loss of DNA binding and STAT3 a inhibition properties	[42]
4	Cu2+ conjugate of synthetic curcumin analogues	Conjugation reaction on the keto-enol moiety	Stronger inhibition of TNF b-induced NF-κB c activation in leukemic KBM-5 cells	[43]
5	Curcumin carbocyclic analogues	Introducing carboxyl group at the diketone moiety	Enhanced antioxidant activity and stronger inhibition of HIV d 1 protease	[44]
6	Semi-carbazone	Introducing NNHCONH2 at the keto-enol moiety	Enhanced antioxidant, antiradical, and antiproliferative activity	[45]

Table II: Examples of recent curcumin delivery systems.

Sr. No	Nano-formulation	Particle Size	Application	Outcome	Reference
1	Curcumin-loaded liposomal PMSA an antibody	100–150 nm	Human prostate cancer (LNCa, C4-2B)	Enhanced antiproliferative efficacy and tar	[46]
2	Curcumin nano-emulsion	<200 nm	Human ovarian adenocarcinoma cells (SKV3)	Increased cytotoxicity	[47]
3	Curcumin loaded liposomes coated with N-dodecyl chitosan-HPTMA chloride	73 nm	Murine fibroblasts (NIH3T3) and murine melanoma (B16F10) cells	Specific toxicity in murine melanoma (but not in fibroblasts)	[47]
4	Liposome-encapsulated curcumin	-	Head & Neck	Cancer growth suppression both in vitro and in vivo	[48]
5	Cancer growth suppression of both in vitro	196 ± 1.4 nm	Rats	Decreased tumor size	[49]

CONCLUSION

Nanocurcumin has great potential in the treatment of various cancers and curcumin, the active ingredient of Curcuma longa extract, has been extensively studied for decades for its anti-inflammatory, antioxidant, and anti-cancer effects. and male hormone resistance. Curcumin has shown significant anti-cancer effects on several different types of cancer, including prostate cancer, breast cancer, colorectal cancer, pancreatic cancer, and head and neck cancer. both in vitro and in vivo. Furthermore, its efficacy and safety in cancer patients alone or combination with other antineoplastic agents have been demonstrated in several human clinical studies. Future preclinical and preclinical studies are needed to obtain in-depth information on curcumin nano-formulation to be transformed into drug candidates for the treatment of cancer(s) alone or in combination. Combination with other treatment modalities and nano curcumin is needed to validate it as a cancer therapy.

Conflicts of interest

There are no conflicts of interest and disclosures regarding the manuscript.

Acknowledgment

The authors express their sincere gratitude to Kamla Nehru College of Pharmacy University Libraries and all other sources for their cooperation and advice in writing this review.

REFERENCES

1. Mukherjee P. Quality control of herbal drugs. 1st ed. Business Horizons Pharmaceutical publisher, 2002; 2.
2. Kokate CK, Purohit AP, Gokhale SB, Pharmacognosy 24th ed. Nirali Prakashan: Pune, 2003; 4-6.
3. Cancercenter.com. (assessed by 29.sep.21).
4. Abruzzo A., Zuccheri G., Belluti F., Provenzano S., Verardi L., Bigucci F.,et al. Chitosan nanoparticles for anticancer drug delivery: development, characterization and in vitro studies on cancer cells. Colloids Surf. B Biointerfaces, 2016; 145: 362–372.
5. HOFFMAN, Robert M.," In-vitro model for HIV and other viral diseases," Patent WO 98/23729, 4 June, Sci. Technol, 1998; 35: 1201–1207.
6. R. Siegel, D. Naishadham, A. Jemal Cancer statistics 2013, CA Cancer J. Clin., 2013; 63: 11-30.
7. C.E. Meacham, S.J. Morrison Tumour heterogeneity and cancer cell plasticity Nature, 2013; 501: 328-337.
8. R. Fisher, L. Pusztai, C. Swanton Cancer heterogeneity: implications for targeted therapeutics Br J Cancer, 2013; 108: 479-485.
9. R.L. Siegel, K.D. Miller, A. Jemal, Cancer statistics, CA Cancer J Clin, 2016; 66: 7-30.
10. D. Schottenfeld, J.F. Fraumeni Jr.Cancer Epidemiology and Prevention Oxford University Press, 2006.
11. K.Y. Yoo, H.R. Shin Cancer epidemiology and prevention Korean J Epidemiol, 2003; 25: 1-15.
12. K. Aizawa, C. Liu, S. Tang, et al. Tobacco carcinogen induces both lung cancer and non-alcoholic steatohepatitis and hepatocellular carcinomas in ferrets which can be attenuated by lycopene supplementation Int J Cancer, 2016; 139: 1171-1181.
13. S.L. Poon, J.R. McPherson, P. Tan, B.T. Teh, S.G. R ozen Mutation signatures of carcinogen exposure: genome-wide detection and new opportunities for cancer prevention Genome Med, 2014; 6: 24.
14. J. Trafialek, W. Kolanowski Dietary exposure to meat-related carcinogenic substances: is there a way to estimate the risk? Int J Food Sci Nutr, 2014; 65: 774-780.
15. M.G. Cumberbatch, A. Cox, D. Teare, J.W. CattoCo ntemporaryoccupational carcinogen exposure and bladder cancer: a systematic review and meta-analysis JAMA Oncol, 2015; 1282-1290.
16. S.O. Antwi, E.C. Eckert, C.V. Sabaque, et al.Exposure to environmental chemicals and heavy metals, and risk of pancreatic cancer Cancer Causes Control, 2015; 26: 1583-1591.
17. D.M. Parkin The global health burden of infection-associated cancers in the year Int J Cancer, 2006; 118: 3030-3044.
18. M. Seto, K. Honma, M. Nakagawa Diversity of genome profiles in malignant lymphoma Cancer Sci, 2010; 101: 573-578.
19. J.C. Cigudosa, N.Z. Parsa, D.C. Louie, etal.Cytogen etic analysis of 363 consecutively ascertained diffuse large B-cell lymphomas Genes, Chromosomes Cancer, 1999; 25: 123-133.
20. E. Shtivelman, B. Lifshitz, R.P. Gale, E. Canaani Fused transcript of abl and bcr genes in chronic myelogenous leukaemia Nature, 1985; 315: 550-554.
21. G. Matlashewski, P. Lamb, D. Pim, J. Peacock, L. C rawford, S. Benchimol Isolation and characterization of a human p53 cDNA clone: expression of the human p53 gene EMBO J, 1984; 3: 3257.
22. Q. Wei, L. Li, D. Chen DNA Repair, Genetic Instability, and Cancer: World Scientific, 2007.
23. R.D. Wood, M. Mitchell, J. Sgouros, T. Lindahl Human DNA repair genes Science, 2001; 291: 1284-1289.
24. E.R. Alvarez-Buylla, Á. Chaos, M. Aldana, et al. Floral morphogenesis: stochastic explorations of a gene network epigenetic landscape PLoS One, 2008; 3: e3626.
25. A. Portela, M. Esteller Epigenetic modifications and human disease Nat Biotechnol, 2010; 28: 1057-1068.
26. S.E. Goelz, B. Vogelstein, S.R. Hamilton, A.P. Fein berg Hypomethylation of DNA from benign and malignant human colon neoplasms Science, 1985; 228: 187-191.
27. M.F. Fraga, E. Ballestar, A. Villar-Garea, et al.Loss of acetylation at Lys16 and trimethylation at Lys20

of histone H4 is a common hallmark of human cancer Nat Genet, 2005; 37: 391-400.
28. S. Sharma, T.K. Kelly, P.A. Jones Epigenetics in cancer Carcinogenesis, 2010; 31: 27-36.
29. Swamy MK, Sinniah UR. Patchouli (Pogostemon cablin Benth.): botany, agrotechnology and biotechnological aspects. Ind Crops Prod, 2016; 87: 161–76.
30. Mohanty SK, Swamy MK, Sinniah UR, Anuradha M. Leptadenia reticulata (Retz.) Wight & Arn. (Jivanti): botanical, agronomical, phytochemical, pharmacological, and biotechnological aspects. Molecules, 2017; 1019: 22.
31. Rodrigues T, Reker D, Schneider P, Schneider G. Counting on natural products for drug design. Nat Chem, 2016; 8: 531.
32. Siddiqui AA, Iram F, Siddiqui S, Sahu K. Role of natural products in drug discovery process. Int J Drug Dev Res., 2014; 6(2): 172–204.
33. Beutler JA. Natural products as a foundation for drug discovery. Curr Prot Pharmacol, 2009; 46(1): 9–11.
34. Thilakarathna SH, Rupasinghe H. Flavonoid bioavailability and attempts for bioavailability enhancement. Nutrients, 2013; 5: 3367–87.
35. Bonifácio BV, da Silva PB, dos Santos Ramos MA, Negri KMS, Bauab TM, Chorilli M. Nanotechnology-based drug delivery systems and herbal medicines: a review. Int J Nanomed, 2014; 9: 1.
36. Watkins R, Wu L, Zhang C, Davis RM, Xu B. Natural product-based nanomedicine: recent advances and issues. Int J Nanomed, 2015; 10: 6055.
37. Martinho N, Damgé C, Reis CP. Recent advances in drug delivery systems. J Biomater Nanobiotechnol, 2011; 2: 510.
38. Jahangirian H, Lemraski EG, Webster TJ, Rafiee-Moghaddam R, Abdollahi Y. A review of drug delivery systems based on nanotechnology and green chemistry: green nanomedicine. Int J Nanomed, 2017; 12: 2957.
39. Yallapu MM, Jaggi M, Chauhan SC. Curcumin nanoformulations: a future nanomedicine for cancer, AAPS, 2017; 1341-1356.
40. Anand P., Kunnumakkara A. B., Newman R. A., Aggarwal B. B. Bioavailability of curcumin problems Mol. Pharm, 2007; 4: 807–818.
41. Cui J, Yu B, Zhao Y, et al. Enhancement of oral absorption of curcumin by self microemulsifying drug delivery systems.Int Pharm, 2009; 354-368.
42. Anand P, Nair HB, Sung B, et al. Design of curcumin-loaded PLGA nanoparticles formulation with enhanced cellular uptake, and increased bioactivity in vitro and superior bioavailability in vitro and superior bioavailability in vivo, Nanotechnol, 2011; 1259–1266.
43. Wang X, Jiang Y, Wang YW, Huang MT, Ho CT, Huang Q. Enhancing anti-inflammation activity of curcumin through O/W nanoemulsions. Food Chem, 2008; 1638-58.
44. Das RK, Kasoju N, Bora U. Encapsulation of curcumin in alginate-chitosan-pluronic composite nanoparticles for delivery to cancer cells.Nano Medicine, 2010; 33(1): 199-207.
45. Teng Z, Luo Y,WangQ.Nanoparticles synthesized from soy protein: preparation, characterization, and application for nutraceutical encapsulation.J Agric Food Chem, 2012; 7(2): 132-141.
46. Jurenka JS,Anti-inflammatory properties of curcumin, a major constituent of Curcuma longa of preclinical and clinical research. Altern Med Rev., 2009; (2): 141-53.
47. Norleena P Gullett ,A R M Ruhul Amin, Soley Bayraktar, John M Pezzuto, Dong M Shin, Fadlo R Khuri, Bharat B Aggarwal, Young-Joon Surh, Omer Kucuk,Cancer prevention with natural compounds. Semin Oncol, 2010; 37(3): 258-81.
48. Reason Wilken Mysore S Veena, Marilene B Wang, Eri S Srivatsan Curcumin is anti-cancer properties and therapeutic activity in head and neck squamous cell carcinoma.Mol Cancer, 2011; 10-1186/1476-4598-10-12.
49. Anindita Mukerjee Jamboor K Vishwanatha Formulation, characterization and evaluation of curcumin-loaded PLGA nanospheres for cancer therapy. Anticancer Res, 2009; (10): 3867-75.