



**FORMULATION, DEVELOPMENT AND EVALUATION OF *CURCUMA LONGA*  
EXTRACT CAPSULES DELIVERY SYSTEM AS AN ADVANCED PHYTOTHERAPY  
APPROACH FOR CANCER**

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Article Received on 22/04/2024

Article Revised on 13/05/2024

Article Accepted on 02/06/2024

**ABSTRACT**

Cancer is a complex disease that is caused by multiple factors and characterized by a rapid and uncontrolled formation of abnormal cells, which may mass together to form a growth or tumor, or proliferate throughout the body, initiating abnormal growth at other sites. Curcuma longa has been used in traditional remedy for a wide range of ailments, including wound healing, urinary and gastrointestinal tract infections, antimalarial, antifungal, anti-inflammatory, antiviral, antibacterial, anaesthetic, chemopreventive, and anticancer, antioxidant, anticoagulant, antifertility, antidiabetic, antiprotozoal, antiviral, antifibrotic, antivenom, antiulcer, Alzheimer's disease, rheumatoid arthritis, hepatoprotective, gastrointestinal tract and cardiovascular system protective effects, and may stimulate immune system, hypocholesterolemic and antihypertensive activities. Curcuma longa was formulated and evaluate as capsules delivery system. It was concluded that the formulation of Curcuma longa extract capsules it was found to be as an optimized capsules according to drug release of Curcuma longa extract capsules delivery system as an advanced phytotherapy approach for cancer.

**KEYWORDS:** Curcuma longa, Extract, Capsules, Anticancer, Phytotherapy.

**INTRODUCTION**

**Background of Anticancer Activity of *Curcuma Longa*<sup>[1-83]</sup>**

Cancer is a complex disease that is caused by multiple factors and characterized by a rapid and uncontrolled formation of abnormal cells, which may mass together to form a growth or tumor, or proliferate throughout the body, initiating abnormal growth at other sites. There are various types of treatment methods, but nowadays researchers are focusing on the use of Traditional Chinese Medicine for the treatment of cancer. Traditional Chinese herbs have a wide range of anticancer activities.

*Curcuma longa* is a perennial and herbaceous plant and medicinal plants from family Zingiberaceae that grows in East Asia, such as China, and India. Turmeric contains a compound named curcumin. Curcumin is a yellow pigment in turmeric that is widely used as a spice, food coloring and preservative.

From the previous studies of Curcuma species, it was found that a number of species have been used in traditional medicine as spices as well as for medical purposes in the treatment of different diseases. The few species such as *Curcuma longa*, have been shown to have anti-inflammatory, and anticancer activity in models of cancer such as inhibit the growth of MCF7 breast cancer cells and colorectal cancer (CRC). In the previous study showed that the formulation topical gel, containing *Curcuma longa*'s derivate, can effectively reduce the oral symptoms of mucositis in patients undergoing head and neck cancer radiotherapy because of its anti-inflammatory and antioxidant effects. Anti-cancer activity of medicinal plant products is included in the texts of Ayurved. Recently they have been studied at experimental and clinical levels in Reverse Pharmacology mode.

In Traditional Indian Medicine Curcumin has been used since thousands of years. Recent studies have demonstrated its numerous activities such as: antimalarial, antifungal, anti-inflammatory, antiviral,

antibacterial, anaesthetic, chemopreventive, and anticancer, antioxidant, anticoagulant, antifertility, antidiabetic, antiprotozoal, antiviral, antifibrotic, antivenom, antiulcer, Alzheimer's disease, rheumatoid arthritis, hepatoprotective, gastrointestinal tract and cardiovascular system protective effects, and may stimulate immune system, hypocholesterolemic and antihypertensive activities. *Curcuma longa* L., reduces HIF-1 levels and function, inhibiting the production of vascular endothelial growth factor (VEGF). Also, curcumin efficiently inhibits the angiogenesis of vascular endothelial cells triggered by hypoxia. Curcumin helps to reduce toxicity of chemotherapy used as anti-cancer drugs and has synergic effects.

Traditional Chinese medicinal plants have a wide range of drug development capacity. These plants have been used since ancient times for the treatment of different diseases, such as heart diseases, intestinal diseases, arthritis, and cancer. *Curcuma longa*, also known as Jianghuang in Chinese was used to derive a flavonoid named Curcumin. According to some studies in India, the rate of various cancers has decreased due to the used of curcumin. Curcumin has been used for the treatment of several diseases, such as cardiac diseases, arthritis, and inflammation.

In the present study the *Curcuma longa* extract powder solid dosage forms were prepared formulation and analyzed in the pre-formulation study of *Curcuma longa* extract capsules delivery system as an advanced phytotherapy approach for cancer.

## MATERIALS AND METHODS

The rhizome's ethanol extract of *Curcuma longa* was prepared and gift from (Prof Dr. Amina El-Shaibany, Professor Dr. of Pharmacognosy, Department of Pharmacognosy, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen). Hard gelatin capsules (Size 0; Color: Red body. Black Cap); Starch, Colloidal Silicon Dioxide (Aerosil), Magnesium Stearate, Sodium Lauryl Sulphate, Hydrochloric Acid (0.1NHCl), pH6.8 buffer Solution, and Ethanol. were obtained from Sigma Aldrich. All chemicals used were all of analytical grade and other materials were gift from (Global Pharmaceutical Industry Company-Yemen).

### Preformulation Study of *Curcuma Longa* Extract

All preformulation tests and studies have been searched by the previous research related to the present research study.<sup>[84]</sup>

### Formulation and Manufacture of The *Curcuma Longa* Capsules<sup>[84-120]</sup>

The selection of the capsule size, the filling machine, the filling method and the excipients were carried out in which 50% of *Curcuma longa* extract mixed with excipients as shown in Table 1, place manually in a separate size "0" capsules, then taken four capsules daily to provide the desired dose.

**Table 1: Formulation of *Curcuma Longa* Capsules.**

Ingredients	Amount(mg) / Capsule
<i>Curcuma Longa</i> Extract	50%
Starch	47.5%
Sodium Lauryl Sulphate	0.5%
Aerosil	1%
Magnesium Stearate	1%

### Evaluation of the Manufactured *Curcuma Longa* Capsules<sup>[84-120]</sup>

#### Determination of Uniformity of Weight and The Amount of Material in The Capsules

For the determination of the uniformity of weight, the British Pharmacopoeia method was used. In which twenty of the *Curcuma longa* capsules prepared as described above were taken at random, their contents individually weighed and the average weight (mass) of the content determined. Not more than two of the individual weights (masses) had to deviate from the average weight (mass) by more than 7.5% and none of the deviates by more than twice that percentage. The amount of powder actually filled into the capsules was also compared with the desired quantity and the difference (in percentage) between the desired and actual quantity calculated. According to the formulation, 50% *Curcuma longa* extract was to be filled in one capsule each. Twenty capsules were thus randomly chosen, their contents weighed, the percentage difference between this and the desired weight calculated and averaged for the 20 capsules to assess the accuracy of the filling process.

#### Determination of The Dissolution Profile of *Curcuma Longa* capsules

In this study the basket method was used. Further, the quantitation of the amount of plant material dissolved was measured based on uv absorbance measured at 425nm, the wavelengths for maximum uv absorption of solutions of the *Curcuma longa* extract determined by using a uv- vis spectrophotometer.

## RESULTS AND DISCUSSION

### Uniformity of Weight and Content of The Capsules

The results of the uniformity of weight and content of the *Curcuma longa* capsules the average deviation in weight from average for *Curcuma longa* capsules were 0.87% and amount of content of capsule was 100.11%, respectively.

According to the British Pharmacopoeia, the limit on the acceptable deviation in weight from average for capsules is  $\pm 8.7\%$  and the limits on the amount of content in the capsules 99% to 102%. The afore-mentioned results thus indicated that the *Curcuma longa* capsules met the British Pharmacopoeia specifications.

**Dissolution Profile of *Curcuma Longa* Capsules****Table 2: Drug Release Percentage of *Curcuma Longa* Capsules.**

Time (min)	Drug Release%
15	45.16%
30	50.10%
45	59.15%
60	60.08%

The results of the dissolution studies on the *Curcuma longa* capsules are shown in Table 2 showed that >50% of the *Curcuma longa* capsule contents dissolved in the dissolution medium within 45 minutes.

**CONCLUSION**

It was concluded that the formulation of *Curcuma longa* extract capsules it was found to be as an optimized capsules according to drug release of *Curcuma longa* extract capsules delivery system as an advanced phytotherapy approach for cancer.

**ACKNOWLEDGEMENT**

The authors are thankful to Global Pharmaceutical Industry Company-Yemen, for providing the research facilities.

**REFERENCES**

- Kaefer CM, Milne JA. The Role of Herbs and Spices in Cancer Prevention. *J Nutr Biochem.*, 2008; 19(6): 347-361.
- Kapoor LD. Handbook of Ayurvedic Medicinal Plants. Boca Raton, FL: CRC Press, 1990.
- Bijauliya RK, Alok S, Singh M, Mishra SB. A Comprehensive Review on Cancer and Anticancer Herbal Drugs. *Int J Pharm Sci Res.*, 2017; 8(7): 2740-2761.
- Singh S, Sharma B, Kanwar S, Kumar A. Lead Phytochemicals for Anticancer Drug Development. *Front Plant Sci.*, 2016; 7: 1667.
- ASEAN. Standard of ASEAN Herbal Medicine. Jakarta: ASEAN Countries, 1993.
- Park SK, et al. Cancer Chemo Protective Effects of *Curcuma Xanthorrhiza*. *Phytother Res.*, 2008; 22(5): 695-698.
- Bruneton J. Pharmacology, Phytochemistry, Medicinal Plants. Paris: Lavoisier, 1995.
- Karsono AH, Mayasari O, Tandrasasmita, Tjandrawinata RR. Molecular Effects of Bioactive Fraction of *Curcuma Mangga* (DLBS4847) as a Down Regulator of 5 $\alpha$ -Reductase Activity Pathways in Prostatic Epithelial Cells. *Cancer Manag Res.*, 2014; 6: 267-278.
- Sreejayan N, Rao MNA, Priyadarsini KI, Devasagayam TP. Inhibition of Radiation Induced Lipid Peroxidation by Curcumin. *Int J Pharm.*, 1997; (151):127-130.
- Malek SN, et al. Nonaqueous Extracts of *Curcuma Mangga* Rhizomes Induced Cell Death in Human Colorectal Adenocarcinoma Cell Line (HT29) Via Induction of Apoptosis and Cell Cycle Arrest at G0/G1 Phase. *Asian Pac J Trop Med.*, 2016; 9(1): 8-18.
- Ruby J, Kuttan G, Babu KD, Rajashekharan KN, Kuttan R. Antitumor and Oxidant Activity of Natural Curcuminoids. *Cancer Lett.*, 1995; (94): 79-83.
- Priyadarsini KI. Free Radical Reactions of Curcumin in Membrane Models. *Free Radic Biol Med.*, 1997; 23(6): 838-43.
- Lattmann E, et al. Anticancer Effects of *Curcuma C20-Dialdehyde* Against Colon and Cervical Cancer Cell Lines. *Asian Pac J Cancer Prev.*, 2015; 16(15): 6513- 6519.
- Reddy AC, Lokesh BR. Studies on the inhibitory Effects of Curcumin and Eugenol on the Formation of Reactive Oxygen Species and the Oxidation of Ferrous Iron. *Mol Cell Biochem.*, 1994; 137(1): 1-8.
- Unnikrishnan MK, Rao MN. Curcumin Inhibits Nitrogen Dioxide Induced Oxidation of Hemoglobin. *Mol Cell Biochem.*, 1995; 146(1): 35-7.
- Pongrakhananon V, Rojanasakul Yon. Anticancer Properties of Curcumin, *Advances in Cancer Therapy.*, 2011.
- Sreejayan N, Rao MN. Nitric Oxide Scavenging by Curcuminoids. *J Pharm Pharmacol.*, 1997; 49(1): 105-7.
- Cronin JR. The Biochemistry of Alternative Medicine, Curcumin Old Spice Is a New Medicine. *Alternative & Complementary Therapies.*, 2003; 34-8.
- Govindrajan VS. Turmeric - Chemistry, Technology and Quality. *CRC Crit Rev Fd Sci Nutr.*, 1980; 12: 199.
- Srimal RC. Turmeric: a Brief Review of Medicinal Properties. *Fitoterapia.*, 1997; LXVIII(6): 483-93.
- WHO. *Rhizoma Curcumae Longae*, WHO Monographs on Selected Medicinal Plants: World Health Organization.
- Ma X, et al. Curcumin Reverses the Effects of Chronic Stress on Behavior, the HPA Axis, BDNF Expression and Phosphorylation of CREB. *Brain Res.*, 2006; 1122(1): 56-64.
- Aggarwal BB, Kumar A, Bharti AC. Anticancer Potential of Curcumin: Preclinical and Clinical Studies. *Anticancer Res.*, 2003; 23(1A): 363- 398.
- Xia X, Cheng G, Pan Y, Xia ZH, Kong L.D. Behavioral, Neurochemical and Neuroendocrine Effects of the Ethanolic Extract from *Curcuma longa* L. in the Mouse Forced Swimming test. *J Ethnopharmacol.*, 2007; 110(2): 356-63.
- Kuroda M, et al. Curcuminoids and Sesquiterpenoids in Turmeric (*Curcuma longa* L.) Suppress an Increase in Blood Glucose Level in Type 2 Diabetic KK-Ay Mice. *J Agric Food Chem.*, 2005; 53(4): 959-63.
- Tsukagawa M, et al. Hypoglycemic Effects of Turmeric (*Curcuma longa* L. rhizomes) on Genetically Diabetic KK-Ay Mice. *Biol Pharm Bull.*, 2005; 28(5): 937-9.

27. Kim MJ, et al. Curcuma Longa Extract Protects Against Gastric Ulcers by Blocking H2 Histamine Receptors. *Biol Pharm Bull.*, 2005; 28(12): 2220-4.
28. Deshpande SS, et al. Subchronic Oral Toxicity of Turmeric and Ethanolic Turmeric Extract in Female Mice and Rats. *Toxicol Lett.*, 1998; 95(3): 183-93.
29. Lee HS. Antiplatelet Property of Curcuma Longa L. Rhizome-Derived ar-Turmerone. *Bioresour Technol.*, 2006; 97(12): 1372-6.
30. Commandeur JN, Vermeulen NP. Cytotoxicity and Cytoprotective Activities of Natural Compounds. The Case of Curcumin. *Xenobiotica.*, 1996; 26(7): 667-80.
31. Soni KB, Rajan A, Kuttan R. Reversal of Aflatoxin Induced Liver Damage by Turmeric and Curcumin. *Cancer Lett.*, 1992; 66(2): 115-21.
32. Azuine MA, Kayal JJ, Bhide SV. Protective Role of Aqueous Turmeric Extract Against Mutagenicity of Direct-Acting Carcinogens as Well as Benzo [alpha] Pyrene-Induced Genotoxicity and Carcinogenicity. *J Cancer Res Clin Oncol.*, 1992; 118(6): 447-52.
33. Kuttan R, Sudheeran PC, Josph CD. Turmeric and Curcumin as Topical Agents in Cancer therapy. *Tumori.*, 1987; 73(1): 29-31.
34. Kuttan R, Bhanumathy P, Nirmala K, George MC. Potential Anticancer Activity of Turmeric (*Curcuma longa*). *Cancer Lett.*, 1985; 29(2): 197-202.
35. Kundu S, Biswas TK, Das P, Kumar S, De DK. Turmeric (*Curcuma longa*) Rhizome Paste and Honey Show Similar Wound Healing Potential: a Preclinical Study in Rabbits. *Int J Low Extrem Wounds.*, 2005; 4(4): 205-13.
36. Charles V, Charles SX. The Use and Efficacy of *Azadirachta Indica* ADR ('Neem') and *Curcuma Longa* ('Turmeric') in Scabies. A Pilot Study. *Trop Geogr Med.*, 1992; 44(1-2): 178-81.
37. Kumar P, et al. Efficacy of Curcumin in the Management of Chronic Anterior Uveitis. *Phytother Res.*, 1999; 13(4): 318-22.
38. Eigner D, Scholz D. *Ferula Asa-Foetida* and *Curcuma Longa* in Traditional Medical Treatment and Diet in Nepal. *J Ethnopharmacol.*, 1999; 67(1): 1-6.
39. Frerichs G, Arends G, Zornig H. *Hagers Handbuch der Pharmazeutischen Praxis*. Berlin: Springer Verlag., 1949.
40. List PH, Horhammer L. *Hagers Handbuch der Pharmazeutischen Praxis*. Berlin: Springer Verlag., 1979.
41. Pozharitskaya ON, Ivanova SA, Shikov AN, Makarov VG. Separation and Free Radical-Scavenging Activity of Major Curcuminoids of *Curcuma Longa* Using HPTCL-DPPH Method. *Phytochemical Analysis.*, 2007; 19(3): 236-43.
42. Li Y, Wo JM, Liu Q, Li X, Martin RCM. Chemoprotective Effects of *Curcuma Aromatica* on Esophageal Carcinogenesis. *Ann Surg Oncol.*, 2009; 16(2): 515-523.
43. Bundy R, Walker AF, Middleton RW, Booth J. Turmeric Extract May Improve Irritable Bowel Syndrome Symptomology in Otherwise Healthy Adults: A Pilot Study. *Journal of Alternative and Complementary Medicine.*, 2004; 10(6): 1015-8.
44. Chainani-Wu N. Safety and Anti-Inflammatory Activity of Curcumin: a Component of Tumeric (*Curcuma longa*). *J Altern Complement Med.*, 2003; 9(1): 161-8.
45. Wu WY, Xu Q, Shi LC, Zhang WB. Inhibitory Effects of *Curcuma Aromatica* Oil on Proliferation of Hepatoma in Mice. *World J Gastroenterol.*, 2000; 6(2): 216-219.
46. Bisset NG. *Herbal Drugs and Phytopharmaceuticals: a Handbook for Practice on a Scientific Basis*. Boca Raton, FL., 1994.
47. Heber D, et al. Curcumin Exerts Multiple Suppressive Effects on Human Breast Carcinoma cells. *Int J Cancer.*, 2002; 98(2): 234-40.
48. Jiang MC, Yang-Yen HF, Yen JJ, Lin JK. Curcumin Induces Apoptosis in Immortalized NIH 3T3 and Malignant Cancer Cell Lines. *Nutr Cancer.*, 1996; 26(1): 111-20.
49. Thaloor D, Singh AK, Sidhu GS, Prasad PV, Kleinman HK, Maheshwari RK. Inhibition of Angiogenic Differentiation of Human Umbilical Vein Endothelial Cells by Curcumin. *Cell Growth Differ.*, 1998; 9(4): 305-12.
50. Sikha A, Harini A, Hegde Prakash L. Pharmacological activities of wild turmeric (*Curcuma aromatica* Salisb): A review. *Journal of Pharmacognosy and Phytochemistry.*, 2015; 3(5): 01-04.
51. Ranjan D, Johnston TD, Wu G, Elliott L, Bondada S, Nagabhushan M. Curcumin Blocks Cyclosporine Aresistant CD28 Costimulatory Pathway of Human T-Cell Proliferation. *J Surg Res.*, 1998; 77(2): 174-8.
52. Limtrakul P, Anuchapreeda S, Lipigorngoson S, Dunn FW. Inhibition of Carcinogen Induced c-Haras and C-Fos Proto-oncogenes Expression by Dietary Curcumin. *BMC Cancer.*, 2001; 1: 1.
53. Fisher C, et al. Curcumin is an In-Vivo Inhibitor of Angiogenesis. *Mol Med.*, 1998; 4(6): 376-83.
54. Kim JA, et al. DiarylHeptanoids with Free Radical Scavenging and Hepatoprotective Activity In-Vitro from *Curcuma Longa*. *Planta Med.*, 2001; 67(9): 876-7.
55. Yu ZF, Kong LD, Chen Y. Antidepressant Activity of Aqueous Extracts of *Curcuma Longa* in Mice. *J Ethnopharmacol.*, 2002; 83(1-2): 161-5.
56. Rajakrishnan V, Menon VP, Rajashekar KN. Protective Role of Curcumin in Ethanol Toxicity. *Phytotherapy research.*, 1998; 12: 55-6.
57. Mohanty I, Arya DS, Gupta SK. Effect of *Curcuma Longa* and *Ocimum Sanctum* on Myocardial Apoptosis in Experimentally Induced Myocardial Ischemic-Reperfusion Injury. *BMC Complement Altern Med.*, 2006; 6: 3.
58. Singh A, Singh SP, Bamezai R. Postnatal Modulation of Hepatic Biotransformation System Enzymes via Translactational Exposure of F1 Mouse

- Pups to Turmeric and Curcumin. *Cancer Lett.*, 1995; 96(1): 87-93.
59. Martin RCG, et al. Hepatic Protection and Anticancer Activity of Curcuma: A Potential Chemo Preventive Strategy Against Hepatocellular Carcinoma. *Int J Oncol.*, 2014; 44(2): 505-513.
  60. Josephson Y, et al. Inhibition of 7,12-dimethylbenz[a]Anthracene (DMBA)-Induced Oral Carcinogenesis in Hamsters by Tea and Curcumin. *Carcinogenesis.*, 2002; 23(8): 1307-13.
  61. Dorai T, Gehani N, Katz A. Therapeutic Potential of Curcumin in Human Prostate Cancer-I. Curcumin Induces Apoptosis in Both Androgen-Dependent and Androgen-Independent Prostate Cancer cells. *Prostate Cancer Prostatic Dis.*, 2000; 3(2): 84-93.
  62. Zhao ZS, O'Brien PJ. The Prevention of CCl4-Induced Liver Necrosis in Mice by Naturally Occurring MethyleneDioxyBenzenes. *Toxicol Appl Pharmacol.*, 1996; 140(2): 411-21.
  63. Soudamini KK, Kuttan R. Inhibition of Chemical Carcinogenesis by Curcumin. *J Ethnopharmacol.*, 1989; 27(1-2): 227-33.
  64. Nagabhushan M, Amonkar AJ, Bhide SV. In-Vitro Antimutagenicity of Curcumin Against Environmental Mutagens. *Food Chem Toxicol.*, 1987; 25(7): 545-7.
  65. Sahu B, Kenwat R, Chandrakar S. Medicinal Value of Curcuma Cassia Roxb: An Overview. *UK J Pharma Biosci.*, 2016; 4(6): 69-74.
  66. Motterlini R, Foresti R, Bassi R, Green CJ. Curcumin, an Antioxidant and Anti-Inflammatory Agent, Induces Heme Oxygenase-1 and Protects Endothelial Cells Against Oxidative Stress. *Free Radic Biol Med.*, 2000; 28(8): 1303-12.
  67. Du Q, et al. Aqueous Extract of Curcuma Aromatica Induces Apoptosis and G2 /M Arrest in Human Colon Carcinoma LS-174-T Cells Independent of p53. *Cancer Biother Radio.*, 2011; 26(1): 97-104.
  68. Donatus IA, Sardjoko, Vermeulen NP. Cytotoxic and Cytoprotective Activities of Curcumin. Effects on Paracetamol-Induced Cytotoxicity, Lipid Peroxidation and Glutathione Depletion in Rat Hepatocytes. *Biochem Pharmacol.*, 1990; 39(12): 1869-75.
  69. Araujo CC, Leon LL. Biological Activities of Curcuma Longa L. *Mem Inst Oswaldo Cruz.*, 2001; 96(5): 723-8.
  70. Wahlstrom B, Blennow G. A Study on the Fate of Curcumin in the Rat. *Acta Pharmacol Toxicol (Copenh).*, 1978; 43(2): 86-92.
  71. Ravindranath V, Chandrasekhara N. Absorption and Tissue Distribution of Curcumin in Rats. *Toxicology.*, 1980; 16(3): 259-65.
  72. Nagabhushan M, Bhide SV. Nonmutagenicity of Curcumin and its Antimutagenic Action Versus Chili and Capsaicin. *Nutr Cancer.*, 1986; 8(3): 201-10.
  73. Vijayalaxmi. Genetic Effects of Turmeric and Curcumin in Mice and Rats. *Mutat Res.*, 1980; 79(2): 125-32.
  74. Kandarkar SV, Sawant SS, Ingle AD, Deshpande SS, Maru GB. Subchronic Oral Hepatotoxicity of Turmeric in Mice-HistoPathological and UltraStructural Studies. *Indian J Exp Biol.*, 1998; 36(7): 675-9.
  75. Roy SN, et al. Antitumor Activity and Antioxidant Property of Curcuma Caesia Against Ehrlich's Ascites Carcinoma Bearing Mice. *Pharm Biol.*, 2013; 51(6): 753-759.
  76. Polasa K, Raghuram TC, Krishna TP, Krishnaswamy K. Effect of Turmeric on Urinary Mutagens in Smokers. *Mutagenesis.*, 1992; 7(2): 107-9.
  77. Prucksunand C, Indrasukhsri B, Leethochawalit M, Hungspreugs K. Phase II Clinical Trial on Effect of the Long Turmeric (*Curcuma longa* Linn) on Healing of Peptic Ulcer. *Southeast Asian J Trop Med Public Health.*, 2001; 32(1): 208-15.
  78. Deodhar SD, Sethi R, Srimal RC. Preliminary Study on Antirheumatic Activity of Curcumin (diferuloyl methane). *Indian J Med Res.*, 1980; 71: 632-4.
  79. Shen TS, et al. Phase I Clinical Ttrial of Curcumin, a Chemopreventive Agent, in Patients with High-Risk or Pre-malignant Lesions. *Anticancer Res.*, 2001; 21(4B): 2895-900.
  80. German Commission E Monograph. *Curcumae longae rhizoma: Bundesanzeiger*, 1985.
  81. Deters M, Siegers C, Hänsel W, Schneider KP, Hennighausen G. Influence of Curcumin on Cyclosporin Induced Reduction of Biliary Bilirubin and Cholesterol Excretion and on Biliary Excretion of Cyclosporin and its Metabolites. *Planta Med.*, 2000; 66: 429-34.
  82. Ammon HP, Wahi MA. Pharmacology of Curcuma Longa. *Planta Med.*, 1991; 57(1): 1-7.
  83. Ramprasad C, Sirsi M. Curcuma Longa and Bile Secretion - Quantitative Changes in the Bile Constituents Induced by Sodium Curcuminatate. *J Sci Industr Res.*, 1957; 16C: 108-10.
  84. Alburyhi MM, El-Shaibany A. Formulation and Evaluation of Anti-peptic Ulcer Capsules of Curcuma Longa Herbal Product. *World Journal of Pharmaceutical Research.*, 2023; 12(22): 76-96.
  85. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Aloe Vera Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Controlling Diabetes. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2024; 13(4): 1408-1423.
  86. Alburyhi MM, Saif AA, Noman MA, Al khawlani MA. Formulation and Evaluation of Bisoprolol Fast Dissolving Tablets. *World Journal of Pharmaceutical Research.*, 2023; 12(16): 01-10.
  87. Hamidaddin MA, Alburyhi MM, Noman MA, Saif AA. Formulation and Evaluation of Rosuvastatin Fast Dissolving Tablets. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2023; 12(9): 2293-2303.
  88. Alburyhi MM, Saif AA, Noman MA, Al Ghoury AA. Formulation and Evaluation of Antimalarial

- Drugs Suppositories. *World Journal of Pharmaceutical Research.*, 2023; 12(20): 89-108.
89. Alburyhi MM, Saif AA, Noman MA, Salim YA, Hamidaddin MA. Formulation and Evaluation of Lisinopril Orally Disintegrating Tablets. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2023; 12(9): 357-369.
90. Alburyhi MM, Saif AA, Noman MA. Stability Study of Six Brands of Amoxicillin Trihydrate and Clavulanic Acid Oral Suspension Present in Yemen Markets. *Journal of Chemical Pharm Research.*, 2013; 5(5): 293-296.
91. Saif AA, Alburyhi MM, Noman MA. Evaluation of Vitamin and Mineral Tablets and Capsules in Yemen Market. *Journal of Chemical Pharm Research.*, 2013; 5(9): 15-26.
92. Alburyhi MM, Saif AA, Noman MA, Al-Ghorafi MA. Comparative Study of Certain Commercially Available Brands of Paracetamol Tablets in Sana'a City, Yemen. *European Journal of Pharmaceutical and Medical Research.*, 2018; 5(12): 36-42.
93. Alburyhi MM, Saif AA, Saif RM. Preformulation Study of Ceftriaxone and Ciprofloxacin for Lipid Based Drug Delivery Systems. *EJUA-BA.*, 2022; 3(4): 339-350.
94. Bary AA, El-Gazayerly ON, Alburyhi MM. Formulation of Immediate Release Lamotrigine Tablets and Bioequivalence Study. *Journal of Chemical Pharm Research.*, 2013; 5(10): 266-271.
95. Alburyhi MM, Saif AA, Noman MA, Saif RM. Recent Innovations of Delivery Systems for Antimicrobial Susceptibility Study of Ciprofloxacin Biodegradable Formulations for Post-Operative Infection Prophylaxis. *European Journal of Pharmaceutical and Medical Research.*, 2023; 10(9): 32-36.
96. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Tribulus Terrestris Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Controlling Diabetes. *World Journal of Pharmaceutical Research.*, 2024; 13(7): 1264-1282.
97. Saif AA, Alburyhi MM, Noman MA, Almaktari AM. Formulation and Evaluation of Trimetazidine Hydrochloride and Clopidogrel Bisulphate Multi-Unit Solid Dosage Forms. *Journal of Chemical Pharm Research.*, 2014; 6(2): 421-426.
98. Alburyhi MM, Saif AA, Noman MA, Saif RM. Recent Innovations of Delivery Systems for Antimicrobial Susceptibility Study of Ceftriaxone Biodegradable Formulations for Post-Operative Infection Prophylaxis. *European Journal of Pharmaceutical and Medical Research.*, 2023; 10(8): 95-99.
99. Alburyhi MM, El-Shaibany A. Formulation and Evaluation of Antitumor Activity of Artemisia Arborescence Extract Capsules as Dietary Supplement Herbal Product Against Breast Cancer. *World Journal of Pharmaceutical Research.*, 2024; 13(3): 95-114.
100. Alburyhi MM, Hamidaddin MA, Saif AA, Noman MA. Formulation and Evaluation of Rivaroxaban Orodispersible Tablets. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2024; 13(2): 2066-2092.
101. Alburyhi MM, Noman MA, Saif AA, Al-Ghorafi MA, Al Khawlani MA, Yahya TA. Formulation and Evaluation of Anti-acne Spironolactone Emulgel Novel Trend in Topical Drug Delivery System. *World Journal of Pharmaceutical Research.*, 2023; 12(22): 96-119.
102. Alburyhi MM, El-Shaibany A. Formulation and Evaluation of Effervescent Granules of Artemisia Arborescence Herbal Product for Foodborne Illness. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2023; 12(12): 1429-1444.
103. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Aloe Rubroviolaceae Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Hepatoprotective. *European Journal of Biomedical and Pharmaceutical Sciences.*, 2024; 11(4): 53-61.
104. Saif AA, Alburyhi MM, Noman MA. Formulation and Evaluation of Ketoprofen Fast Dissolving Tablets. *International Journal of Sciences.*, 2018; 7(09): 27- 39.
105. Alburyhi MM, Saif AA, Noman MA, Hamidaddin MA. Formulation and Evaluation of Clopidogrel Orodispersible Tablets. *World Journal of Pharmaceutical Research.*, 2024; 13(6): 42-64.
106. Alburyhi MM, Saif AA, Noman MA, Yahya TA. Formulation, Development and Evaluation of Famotidine Orodispersible Tablets. *European Journal of Pharmaceutical and Medical Research.*, 2023; 10(10): 56-62.
107. Noman MA, Alburyhi MM, El-Shaibany A, Alwesabi NA. Preformulation and Characterization Studies of Pandanus Odoratissimus L Extract Active Ingredient in Treatment of Nocturnal Enuresis. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2024; 13(2): 1603-1620.
108. Alburyhi MM, El-Shaibany A. Formulation and Evaluation of Antibacterial Orodispersible Tablets of Artemisia Arborescence Extract Herbal Product. *European Journal of Pharmaceutical and Medical Research.*, 2024; 11(2): 409-417.
109. Alburyhi MM, Saif AA, Noman MA, Yassin SH. Formulation and Evaluation of Simvastatin Orodispersible Tablets. *World Journal of Pharmaceutical Research.*, 2023; 12(16): 1033-1047.
110. Othman AM, Alburyhi MM, Al-Hadad GH. Formulation and Evaluation of Captopril Mouth Dissolving Tablets. *European Journal of Pharmaceutical and Medical Research.*, 2024; 11(1): 18-28.
111. Alburyhi MM, El-Shaibany A. Formulation and Evaluation of Oral Pharmaceutical Solution of Pandanus Odoratissimus L Extract Herbal Product in Treatment of Nocturnal Enuresis. *World Journal of*

- Pharmacy and Pharmaceutical Sciences., 2024; 13(1): 1840-1851.
112. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Pandanus Odoratissimus Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Hepatoprotective. *European Journal of Pharmaceutical and Medical Research.*, 2024; 11(4): 06-13.
  113. Alburyhi MM, Saif AA, Noman MA, Yahya TA, Al-Ghorafi MA. Formulation and Evaluation of Drotaverine Orally Disintegrating Tablets. *World Journal of Pharmaceutical Research.*, 2023; 12(18): 66-79.
  114. Noman MA, Alburyhi MM, Alqubati MA. Preformulation and Characterization Studies of Clopidogrel Active Ingredient for Orodispersible Tablets Development. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2024; 13(3): 996-1015.
  115. Noman MA, Alburyhi MM, El-Shaibany A, Alwesabi NA. Formulation and Evaluation of Pandanus Odoratissimus L Extract for Treatment of Nocturnal Enuresis as Orodispersible Tablets Delivery System. *World Journal of Pharmaceutical Research.*, 2024; 13(5): 56-71.
  116. Alburyhi MM, Saif AA, Noman MA. Formulation and Evaluation of Ticagrelor Orodispersible Tablets. *World Journal of Pharmaceutical Research.*, 2024; 13(5): 26-55.
  117. Alburyhi MM, Noman MA, Saif AA, Salim YA, Abdullah JH. Formulation and Evaluation of Domperidone Orodispersible Tablets. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2024; 13(3): 49-68.
  118. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Dictyota Dichotoma Extract Medicinal Seaweed Capsules Delivery System as an Advanced Phytotherapy Approach for Cancer. *European Journal of Biomedical and Pharmaceutical Sciences.*, 2024; 11(4): 63-70.
  119. Aboghanem A, Alburyhi MM, Noman MA. Effect of Different Excipients on Formulation of Immediate Release Artemether/Lumefantrine Tablets. *Journal of Chemical Pharm Research.*, 2013; 5(11): 617-625.
  120. Alburyhi MM, Saif AA, Noman MA, Saeed SA, Al-Ghorafi MA. Formulation and Evaluation of Diclofenac Orodispersible Tablets. *European Journal of Pharmaceutical and Medical Research.*, 2023; 10(9): 01-06.