Biochemistry & Molecular Biology Letters
ISSN: 2454-9304

Biochemistry & Molecular Biology Letters

Research | Vol 3 Iss 1

Drug Profile of Dasatinib

Suresh M*, Kavya R, Naveen R, Karthik M

Department of Pharmaceutics, Production Department, Jawaharlal Nehru Technological University, Hyderabad, India

***Corresponding author:** Suresh M, Department of Pharmaceutics, Production Department, Jawaharlal Nehru Technological University, Hyderabad, India, E-mail: Sureshmuthyala@gmail.com

Received: March 08, 2017; **Accepted:** March 16, 2017; **Published:** March 29, 2017

Abstract

Many patients find it difficult to swallow tablets and hard gelatin capsules and thus not comply with prescription that results in high incidence of non-compliance and ineffective therapy. Immediate release tablets are gaining prominence as new drug delivery systems. These dosage forms dissolve or disintegrate in oral cavity within a minute without the need of water or chewing. In this study, an effort has been made to formulate immediate release tablets using different disintegrants drug. Considering the merits of Dasatinib, we are proposing to choose it as an anticancer drug.

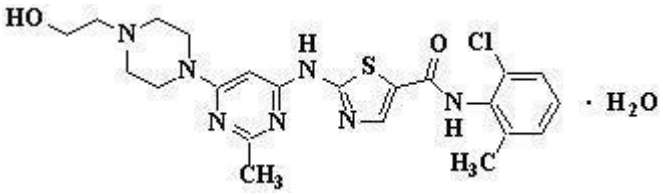
Keywords: Silybum marianum; Dasatinib; Microsomes; Homogenate

Introduction

Drug Name: Dasatinib

Category: Anti cancer agent

Chemical structure:



IUPAC Name: N-(2-chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)-1-piperazinyl]-2-methyl-4-pyrimidinyl] amino]-5-thiazolecarboxamide, monohydrate

Molecular Formula: C22H26ClN7O2S • H2O

Molecular Weight: 506.02 (monohydrate), 488.01 (anhydrous)

Half life: 1.3 to 5 hrs

Dosage forms and Strengths: Tablets: 20 mg, 50 mg, 70 mg, 80 mg, 100 mg, and 140 mg.

Description: crystalline white powder

Solubility: It is poorly soluble in water and slightly soluble in acetone, acetonitrile, ethanol, methanol, polyethylene glycol.

Citation: Suresh M, Kavya R, Naveen R, et al. Antioxidant Effect of Silymarin During Non-Enzymatic Peroxidation of Rat Kidney Microsomes and Mitochondria. Biochem Mol Biol Lett. 2017;3(1):110.

Melting point: 280°–286° C

Mechanism of Action: Dasatinib, at nanomolar concentrations, inhibits the following kinases: BCR-ABL, SRC family (SRC, LCK, YES, FYN), c-KIT, EPHA2, and PDGFRβ. Dasatinib is predicted to bind to multiple conformations of the ABL kinase. Dasatinib inhibited the growth of chronic myeloid leukemia (CML) and acute lymphoblastic leukemia (ALL) cell lines overexpressing BCR-ABL. Dasatinib was able to overcome imatinib resistance resulting from BCR-ABL kinase domain mutations, activation of alternate signaling pathways involving the SRC family kinases (LYN, HCK), and multi-drug resistance gene overexpression.

Pharmacokinetics

Absorption: Maximum plasma concentrations (Cmax) of dasatinib are observed between 0.5 and 6 hours following oral administration.

Distribution: It has a large apparent volume of distribution (2505 L). This indicates that the drug is extensively distributed in extra vascular space. Protein binding is 96 %.

Metabolism: Dasatinib is extensively metabolized in humans, primarily by the cytochrome P450 enzyme 3A4. CYP3A4 was the primary enzyme responsible for the formation of the active metabolite. Other enzymes involved are Flavin-containing monooxygenase 3 (FMO-3) and uridine diphosphate-glucuronosyltransferase (UGT) enzymes.

Excretion: Dasatinib is excreted mainly in faeces (85%) and urine (4%).

Uses: It is indicated for the treatment of adults with chronic, accelerated, or myeloid or lymphoid blast phase chronic myeloid leukemia with resistance or intolerance to prior therapy including imatinib.

It is also indicated for the treatment of adults with Philadelphia chromosome-positive acute lymphoblastic leukemia with resistance or intolerance to prior therapy.

Side Effects

Hematologic:
Thrombocytopenia
Anemia
Neutropenia
Hemorrhage
Neutropenia

General:
Pain
Fatigue
Abdominal pain
Mucosal inflammation
Decreased weight
Chest pain

Gastrointestinal:
Gastrointestinal side effects including diarrhea (49%), nausea (34%), vomiting (22%), anorexia (19%), gastrointestinal bleeding (14%), and constipation (14%) have been reported.

Nervous system:
Nervous system side effects including headache (40%), neuropathy (including peripheral neuropathy) (13%), and CNS bleeding (2%) have been reported

Musculoskeletal:
Musculoskeletal side effects including musculoskeletal pain (39%), arthralgia (19%), and myalgia (12%) have been reported.

Respiratory:

Respiratory side effects have included dyspnea (32%), cough (28%), upper respiratory tract infection/inflammation (26%), bacterial, viral, and fungal pneumonia (11%), pulmonary edema (4%), and pulmonary hypertension (1%).

Metabolic:

Metabolic side effects including hypophosphatemia (up to 23%) and hypocalcemia (up to 20%) have been reported. Appetite disturbances and hyperuricemia have been reported frequently. Hypoalbuminemia has been reported infrequently.

Hepatic:

Hepatic side effects including elevated SGPT (ALT) (up to 11%), elevated SGOT (AST) (up to 8%), elevated bilirubin (up to 8%), and elevated transaminase have been reported. Cholecystitis, cholestasis, and hepatitis have been reported infrequently.

Cardiovascular:

Cardiovascular side effects including arrhythmia (11%) and pericardial effusion (4%) have been reported. Palpitations, flushing, hypotension, hypertension, angina pectoris, cardiomegaly, and myocardial infarction have been reported frequently. Pericarditis, ventricular tachycardia, acute coronary syndrome, myocarditis, and QT prolongation have been reported infrequently. Congestive heart failure/cardiac dysfunction (4%) has included ventricular dysfunction, cardiac failure, cardiac failure congestive, cardiomyopathy, and congestive cardiomyopathy, ejection fraction decreased, and left ventricular failure.

Dermatologic:

Dermatologic side effects including pruritus (11%) have been reported. Hyperhidrosis, alopecia, dry skin, acne, urticaria, dermatitis (including eczema), photosensitivity reaction, nail disorder, and pigmentation disorder have been reported frequently. Skin ulcer, acute febrile neutrophilic dermatosis, bullous conditions, livedo reticularis, panniculitis, palmar-plantar erythrodysesthesia syndrome have been reported infrequently. Skin rash (35%) has included erythema, exfoliative rash, generalized erythema, milia, rash, erythematous rash, follicular rash, generalized rash, macular rash, maculopapular rash, papular rash, pruritic rash, pustular rash, skin exfoliation, systemic lupus erythematosus rash, vesiculosa urticaria, drug eruption, and vesicular rash.

Renal:

Renal side effects including elevated creatinine (up to 2%) have been reported. Urinary frequency and renal failure have been reported frequently. Proteinuria has been reported infrequently.

Other:

Other side effects including infection (including bacterial, viral, fungal, and non-specified), herpes virus infection, sepsis (including fatal outcomes), enterocolitis infection, tinnitus, vertigo, and contusion have been reported frequently. Blood creatine phosphokinase increased has also been reported.

Psychiatric:

Psychiatric side effects including insomnia, depression, anxiety, confusional state, and affect lability have been reported frequently. Decreased libido has been reported infrequently.

Genitourinary:

Genitourinary side effects including gynecomastia have been reported frequently. Irregular menstruation has been reported infrequently.

Hypersensitivity:

Hypersensitivity side effects have infrequently included erythema nodosum.

Ocular:

Ocular side effects including visual disorder, conjunctivitis, and dry eyes have been reported frequently.

Oncologic:

Oncologic side effects including tumor lysis syndrome have been reported frequently.

Drug Interactions

CYP3A4 Inhibitors: May increase dasatinib drug levels and should be avoided. If co administration cannot be avoided, monitor closely.

CYP3A4 Inducers: May decrease dasatinib drug levels. If co administration cannot be avoided, consider increasing dasatinib dose.

Antacids: May decrease dasatinib drug levels. Avoid simultaneous administration. If needed, administer the antacid at least 2 hours prior to or 2 hours after the dose of dasatinib

H2 Antagonists/Proton Pump Inhibitors: May decrease dasatinib drug levels.

Storage: Dasatinib should be stored at room temperature between 15-300ºC (59-86 F).

Conclusion

Various formulation trails of dasatinib tablets were conducted using three super disintegrants like Croscarmellose sodium, sodium starch glycolate and crospovidone. These three super disintegrants were used at three different concentrations like 2.5%, 3.5% and 4.5%. Performed 9 formulation trials were done. In that various preformulation parameters were conducted that which has given two good results that which were present within the limit as per B.P.

REFERENCES

1. Matilda AA. Review on Ophthalmology using Nanotechnology. J Nanomed Nanotechnol. 2015;6:272.
2. Wu. Using Glucose-bound Fe3O4 Magnetic Nanoparticles as Photothermal Agents for Targeted Hyperthermia of Cancer Cells. J Nanomed Nanotechnol. 2015;5:264.
3. Fujinami N. Enhancing the Anti-Tumor Effects of Cancer Peptide Vaccine Therapy. J Vaccines Vaccin. 2016;7:330.
4. Abdelhalim MAK. Lung Tissue Alterations were Size-dependent with Smaller Ones Induced More Effects and Related with Time Exposure of Gold Nanoparticles. J Cancer Sci Ther. 2012;4:6.
5. Qiu L. Rational Design of Synthetic Polymers as Drug Carriers for Cancer Therapy. J Mol Pharm Org Process Res. 2013;1:e101.
6. Gowda R. Use of Nanotechnology to Develop Multi-Drug Inhibitors for Cancer Therapy. J Nanomed Nanotechnol. 2013;4:184.
7. Khan RD. The Use of Nanocarriers for Drug Delivery in Cancer Therapy. J Cancer Sci Ther. 2010;2:058-062.
8. Henare K, Ching LM. The Potential of STING Agonists for Re-Polarizing Macrophages as an Approach to Cancer Therapy. J Clin Cell Immunol. 2015;6:325.
9. Kumar S. Drug Targets for Cancer Treatment: An Overview. Med Chem. 2015;5:115.
10. Ahmed AH. EDL-360: A Potential Novel Antiglioma Agent. J Cancer Sci Ther. 2014;6:370-377.
11. Patel S. Nanotechnology in Healthcare: Applications and Challenges. Med Chem. 2015; 5:528-533.
12. Maroof K. Scope of Nanotechnology in Drug Delivery. J Bioequiv Availab. 2016;8:001-005.
13. Guo P. Studies and application of Nanomotor for Single Pore Sensing, Single Fluorescence Imaging, and RNA Nanotechnology. Biochem Anal Biochem 2015;4:i105.
14. Maroof K. Scope of Nanotechnology in Drug Delivery. J Bioequiv Availab. 2016;8:001-005.
15. Upadhyay S, Wonders of Nanotechnology in the Treatment for Chronic Lung Diseases. J Nanomed Nanotechnol 2015;6:337.
16. Lloyd-Hughes H, Current and Future Nanotechnology Applications in the Management of Melanoma: A Review. J Nanomed Nanotechnol. 2015;6:334.
17. Dennis E. Utilizing Nanotechnology to Combat Malaria. J Infect Dis Ther. 2015;3:229.
18. Menaa F. Genetic Engineering and Nanotechnology: When Science-Fiction Meets Reality! Adv Genet Eng. 2015;4:128.
19. Satapathy MK. Shaping Safer Future Nanotechnology through Wise Worthy Scientific Research. J Bioprocess Biotech 2015;5:243.
20. Khetawat S. Nanotechnology (Nanohydroxyapatite Crystals): Recent Advancement in Treatment of Dentinal Hypersensitivity. J Interdiscipl Med Dent Sci. 2015;3:181.
21. Arif T. Therapeutic and Diagnostic Applications of Nanotechnology in Dermatology and Cosmetics. J Nanomedine Biotherapeutic Discov 2015;5:134.

22. Singh RK. Development of a Nanotechnology Based Biomedicine RISUG-M as a Female Contraceptive in India. J Nanomed Nanotechnol 2015;6:297.
23. Rakesh M, Applications of Nanotechnology. J Nanomedine Biotherapeutic Discov. 2015;5:131.
24. Yadav SK. Nanotechnology: A Spark to the Use of Plant Origin Bioactive Compounds in Therapeutics. Single Cell Biol. 2015;4:108.
25. Syduzzaman, l. Smart Textiles and Nano-Technology: A General Overview. J Textile Sci Eng. 2015;5:181.
26. Bhandare N, Narayana A. Applications of Nanotechnology in Cancer: A Literature Review of Imaging and Treatment. J Nucl Med Radiat Ther. 2014;5:195.
27. Anusha PN, Siddiqui A. Nanomedical Platform for Drug Delivery. J Nanomedic Nanotechnol. 2011;2:122.
28. Douroumis D. Mesoporous silica Nanoparticles as Drug Delivery System. J Nanomed Nanotechnol. 2011;2:102e.
29. Naga AP, Siddiqui A. Nanomedical Platform for Drug Delivery. J Nanomedic Nanotechnol. 2011;2:122.
30. Al-Achi A and Lawrence JBS. Micelles: Chemotherapeutic Drug Delivery. Clin Pharmacol Biopharm 2013;2:e114.
31. Vivero-Escoto JL. Nanovehicles for Intracellular Protein Delivery. J Biotechnol Biomater 2013;3:e117.
32. Nirmala MJ, Nagarajan R. Microemulsions as Potent Drug Delivery Systems. J Nanomed Nanotechnol. 2016;7:e139.
33. Mandal B. Personalized Nanotheranotics for Cancer. J Biotechnol Biomater. 2016;6:e127.
34. Zaman HH. Addressing Solubility through Nano Based Drug Delivery Systems. J Nanomed Nanotechnol. 2016;7:376.
35. Koushik OS. Nano Drug Delivery Systems to Overcome Cancer Drug Resistance - A Review. J Nanomed Nanotechnol. 2016;7:378.
36. Patil J. Encapsulation Technology: Opportunity to develop Novel Drug Delivery Systems. J Pharmacovigil 2016;4:e157.
37. Shanmugan P, Bandameedi R. Chronotherapeutic Drug Delivery Systems. J Drug Metab Toxicol. 2015;6:194.
38. Colone M. Redox-active Microcapsules as Drug Delivery System in Breast Cancer Cells and Spheroids. J Mol Genet Med. 2016;10:200.
39. Van Tilburg CWJ. Spinal Analgesic Drug Delivery for Ehlers-Danlos Hypermobility Type Chronic Pain Treatment: A Case Report. J Pain Relief. 2016;5:235.
40. AbouAitah KEA. Mesoporous Silica Materials in Drug Delivery System: pH/Glutathione- Responsive Release of Poorly Water-Soluble Pro-drug Quercetin from Two and Three-dimensional Pore-Structure Nanoparticles. J Nanomed Nanotechnol. 2016;7:360.
41. Dudhipala N. Amoxycillin Trihydrate Floating-Bioadhesive Drug Delivery System for Eradication of Helicobacter pylori: Preparation, In Vitro and Ex Vivo Evaluation. J Bioequiv Availab. 2016;8:118-124.
42. Patil J. Hydrodynamically Balanced Gastro-Retentive Site Specific Drug Delivery System: An Innovative Approach. J Pharmacovigil. 2015;3:e146.
43. AbouAitah KEA. Mesoporous Silica Materials in Drug Delivery System: pH/Glutathione- Responsive Release of Poorly Water-Soluble Pro-drug Quercetin from Two and Three-dimensional Pore-Structure Nanoparticles. J Nanomed Nanotechnol 2016;7:360.
44. Bhasin S, Patel R. Enhanced Oral Bioavailability of Alitretinoin by Lipid Drug Delivery System. Pharm Anal Acta. 2015;6:433.
45. Jethara SI, Patel MR. Optimizing Oral Controlled Release Drug Delivery Systems using Experimental Designs. Intel Prop Rights. 2015;3:135.
46. Patil JS. Novel Drug Delivery Strategies: New Concepts. Adv Pharmacoepidemiol Drug Saf. 2015;4:e134.
47. Jethara SI, Patel MR. Optimizing Oral Controlled Release Drug Delivery Systems Using Experimental Designs. Intel Prop Rights. 2015;3:142.
48. Farooq U. Design and Development of Multi Particulate System for Targeted Drug Delivery Using Natural Polymer. Pharm Anal Acta. 2015;6:366.
49. Saboktakin MR. pH Sensitive Chitosan-based Supramolecular Gel for Oral Drug Delivery of Insulin. J Mol Genet Med. 2015;9:170.

50. Kumar V. Nanostructures for Drug Delivery. J Drug Metab Toxicol. 2015; 6: e125.
51. Wu C. Using Glucose-bound Fe3O4 Magnetic Nanoparticles as Photothermal Agents for Targeted Hyperthermia of Cancer Cells. J Nanomed Nanotechnol. 2015;5:264.
52. Shroff K, Vidyasagar A. Polymer Nanoparticles: Newer Strategies towards Targeted Cancer Therapy. J Phys Chem Biophys.2013;3:125.
53. Alaqad K, Saleh TA. Gold and Silver Nanoparticles: Synthesis Methods, Characterization Routes and Applications towards Drugs. J Environ Anal Toxicol. 2016;6:384.
54. Heidari A. Pharmacogenomics and Pharmacoproteomics Studies of Phosphodiesterase-5 (PDE5) Inhibitors and Paclitaxel Albumin-stabilized Nanoparticles as Sandwiched Anti-cancer Nano Drugs between Two DNA/RNA Molecules of Human Cancer Cells. J Pharmacogenomics Pharmacoproteomics. 2006;7:e153.
55. Israel LL. Ultrasound-Mediated Surface Engineering of Theranostic Magnetic Nanoparticles: An Effective One-Pot Functionalization Process Using Mixed Polymers for siRNA Delivery. J Nanomed Nanotechnol. 2016;7:385.
56. Heidari A. Novel and Stable Modifications of Intelligent Cadmium Oxide (CdO) Nanoparticles as Anti-Cancer Drug in Formation of Nucleic Acids Complexes for Human Cancer Cells' Treatment. Biochem Pharmacol (Los Angel). 2016;5:207.
57. Prabhakar U. Challenges and key considerations of the enhanced permeability and retention effect for nanomedicine drug delivery in oncology. Cancer research. 2013;73:2412-2417.
58. Jiang W. Advances and challenges of nanotechnology-based drug delivery systems. Expert opinion on drug delivery. 2007;4:621-633.
59. Hughes GA. Nanostructure-mediated drug delivery. Nanomedicine: nanotechnology, biology and medicine 2005;1:22-30.
60. Ravichandran R. Nanotechnology-based drug delivery systems. NanoBiotechnology. 2009;5:17-33.
61. Aminabhavi TM. Polysaccharide-Based Hydrogels as Biomaterials in Drug Delivery. J Pharma Care Health Sys 2015;2:e132.
62. Nasri M, Mirshekarpour H. Polymeric Nanostructures as Colloidal Drug Delivery Systems: Thermosensitive Hydrogels Containing Self-Assembled Micelles. J Nanomed Nanotechnol. 2015;6:301.
63. Patil JS. Hydrogel System: An Approach for Drug Delivery Modulation. Adv Pharmacoepidemiol Drug Saf. 2015;4:e135.
64. Gopi S. Effective Drug Delivery System of Biopolymers Based On Nanomaterials and Hydrogels - A Review. Drug Des. 2016;5:129.
65. Suri SS. Nanotechnology-based drug delivery systems. Journal of Occupational Medicine and Toxicology. 2007;2:1.
66. De Villiers MM. Nanotechnology in drug delivery. Springer Science & Business Media. 2008.
67. Mura S. Stimuli-responsive nanocarriers for drug delivery. Nature materials. 2013;12:991-1003.
68. Wagner V. The emerging nanomedicine landscape. Nature biotechnology. 2016;24:1211-1217.
69. Mishra B. Colloidal nanocarriers: a review on formulation technology, types and applications toward targeted drug delivery. Nanomedicine: Nanotechnol Biol Med. 2010;6:9-24.
70. Park K. Facing the truth about nanotechnology in drug delivery. ACS nano 2013;7:7442-7447.
71. Jain KK. Nanotechnology-based drug delivery for cancer. Technology in cancer research & treatment. 2005;4:407-416.
72. Jain KK. Targeted drug delivery for cancer. Technology in cancer research & treatment. 2005;4:311-313.
73. Sahoo SK. Nanotechnology in ocular drug delivery. Drug discovery today 2008;13:144-151.
74. Thangapazham RL. Evaluation of a nanotechnology-based carrier for delivery of curcumin in prostate cancer cells. Int J Oncology. 2008;32:1119-1124.
75. Cuenca AG. Emerging implications of nanotechnology on cancer diagnostics and therapeutics. Cancer. 2006;107:459-466.

76. Parhi P. Nanotechnology-based combinational drug delivery: an emerging approach for cancer therapy. Drug discovery today 2012;17:1044-1052.
77. Misra R. Cancer nanotechnology: application of nanotechnology in cancer therapy. Drug Discovery Today. 2010;15:842-850.
78. Farrell Dl. Nanotechnology-based cancer therapeutics-promise and challenge-lessons learned through the NCI alliance for nanotechnology in cancer. Pharmaceutical Res. 2011;28:273-278.
79. Cai W. Applications of gold nanoparticles in cancer nanotechnology. Nanotechnology, science and applications. 2008;1.
80. Alexis F. Nanoparticle technologies for cancer therapy. In Drug delivery. Springer Berlin Heidelberg 2010;55-86.
81. Madani SY. A new era of cancer treatment: carbon nanotubes as drug delivery tools. Int J Nanomedicine. 2011;6:2963-2979.
82. Orive G. Micro and nano drug delivery systems in cancer therapy. Cancer Therapy. 2005;3:131-138.
83. Wang M, Thanou M. Targeting nanoparticles to cancer. Pharmacological Research. 2010;62:90-99.
84. Elhissi A. Carbon nanotubes in cancer therapy and drug delivery. Journal of drug delivery. 2012.
85. Jabir NR. Nanotechnology-based approaches in anticancer research. International Journal of Nanomedicine. 2012;7:4391.
86. Subramani K. Targeting nanoparticles as drug delivery systems for cancer treatment. Current Nanoscience. 2009;5:135-140.
87. Khullar O. Image-guided sentinel lymph node mapping and nanotechnology-based nodal treatment in lung cancer using invisible near-infrared fluorescent light. In Seminars in thoracic and cardiovascular surgery. 2010.
88. Alimohammadi YH, Joo SW. PLGA-based nanoparticles as cancer drug delivery systems. Asian Pac J Cancer Prev. 2014; 15: 517-535.
89. Talekar M. Targeting of nanoparticles in cancer: drug delivery and diagnostics. Anti-Cancer Drugs. 2011;22:949-962.
90. Massadeh S. Nano-materials for Gene Therapy: An Efficient Way in Overcoming Challenges of Gene Delivery. J Biosens Bioelectron. 2016;7:195.
91. Watanabe S. Novel Cancer Vaccination System Based on Human Endo-B-NAcetyl Glucosaminidase Gene Delivery. J Glycobiol. 2014;3:106.
92. Porada CD, Almeida-Porada G. Treatment of Hemophilia A in Utero and Postnatally using Sheep as a Model for Cell and Gene Delivery. J Genet Syndr Gene Ther. 2012;S1:011.
93. Arpke RW , Cheng PW. Characterization of Human Serum Albumin-Facilitated Lipofection Gene Delivery Strategy. J Cell Sci Ther 2011;2:108.
94. Nicolini C. From Nanobiotechnology to Organic and Biological Monitoring of Health and Environment for Biosafety. J Bioanal Biomed 2013;5:108-117.
95. Niemeyer CM, Mirkin CA. Nanobiotechnology: concepts, applications and perspectives. John Wiley & Sons 2004;1.
96. Ma P, Mumper RJ. Paclitaxel nano-delivery systems: a comprehensive review. J Nanomed nanotechnol. 2013;4:1000164.
97. Orive G. Micro and nano drug delivery systems in cancer therapy. Cancer Therapy. 2005;3:131-8.
98. Elzoghby AO, Protein-based nanocarriers as promising drug and gene delivery systems. J control rel 2012;161:38-49.
99. Vaze OS. Pharmaceutical Nanocarriers (Liposomes and Micelles) in Cancer Therapy. J Nanomed Nanotechnol 2016;7:e138.
100. Gajbhiye KR. Targeted Brain Delivery of Bioactive Molecules Using Nanocarriers. J Bioequiv Availab 2015;7:112-122.