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Lisinopril- A Review

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ABSTRACT: Lisinopril is a drug belongs to angiotensin converting enzyme{ACE} inhibitor. It is approved by the (FDA)food drug and administration for the management of hypertension in adult and pediatric patients six years and older and as adjunctive therapy in the treatment of heart failure. Lisinopril is also used to treat congestive heart failure in adults, or to improve survival after a heart attack. Lisinopril does not bound to any serum protein and remains unchanged in urine. lisinopril estimation can be done by HPLC, UV visible spectrophotometer and other tritrimetic methods. Zestril and prinvil are the marketed formulations of lisinopril dehydrate tablets.

Keywords: lisinopril, congestive heart failure, heart attack, UV visible spectrophotometer

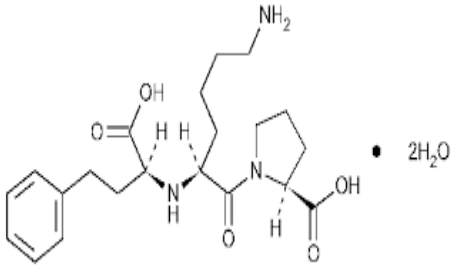
I. INTRODUCTION[1] :

Lisinopril is a synthetic peptide derivative of captopril. It can be administered orally and the bioavailability of this drug is less than 25%.

Lisinopril was patented in 1978, and approved for medical use in the United States in 1987. It is available as a generic medication. In 2017, it was the most commonly prescribed medication in the United States, with more than 104 million prescriptions. In July 2016, lisinopril was approved for use in the United States in the form of oral solution formulation.

STRUCTURE OF LISINOPRIL[2]

Lisinopril is a white to off-white, crystalline powder. It's molecular weight is 441.53. lisinopril is soluble in water and sparingly soluble in methanol and practically insoluble in ethanol. It is chemically described as (S)-1-[N2-(1-carboxy-3-phenylpropyl)-Llysyl]-L-proline dihydrate. Its empirical formula is C21H31N3O5 . 2H2O



Structure of lisinopril

MECHANISM OF ACTION OF LISINOPRIL [3]

Lisinopril prevents the conversion of angiotensin I to angiotensin II, which is a potent vasoconstrictor. A decrease in angiotensin II eventually causes a reduction in aldosterone secretion, which causes in decrease sodium reabsorption in the collecting duct and decreases potassium excretion that may result in increase in serum potassium.

PHARMACOKINETICS[4,5] :

Lisinopril is slowly and incompletely absorbed after oral doses.On an average about 25% of the drug is absorbed, but the absorption varies considerably between individuals, ranging from about 6 to 60%. Lisinopril does not appear to bound to other serum proteins. It does not undergo metabolism and excreted unchanged in the urine. The absorption of lisinopril is not influenced by the presence of food in the gastrointestinal tract. The absolute bioavailability of lisinopril is reduced to 16% in patients with stable NYHA Class II-IV congestive heart failure, and the volume of distribution appears to be slightly smaller than that in normal subjects. The patients with acute myocardial infection has oral bioavailability of lisinopril is similar to that in healthy volunteers. Lisinopril exhibits an effective half-life of accumulation of 12 hours, by multiple dosing. Impaired renal function decreases elimination of lisinopril, which is excreted principally through the

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kidneys, but this decrease becomes clinically important only when the glomerular filtration rate is below 30 mL/min. Above this glomerular filtration rate, the elimination half-life is little changed. On average, older people have (approximately doubled) higher blood levels and area under the plasma concentration time curve (AUC) than younger patients.

Absorption: Variable; About 25% of an oral dose is absorbed.
Distribution: Lisinopril is widely distributed in tissues. Plasma protein-binding appears insignificant.
Preclinical studies of the lisinopril indicate that it crosses the placental barrier.
Metabolism: Lisinopril is the water soluble member of ACE inhibitor class and is not metabolized by the liver.

Excretion: Lisinopril is excreted unchanged in the urine.

PHARMACODYNAMICS [4]

Lisinopril inhibits (ACE)angiotensin converting enzyme, by preventing the conversion of angiotensin I to angiotensin II, a potent vasoconstrictor. Reduced formation of angiotensin II decreases peripheral arterial resistance and aldosterone secretion, thereby reducing blood pressure water retention.

INTERACTIONS

1. **Drug-drug interactions :**
Diuretics: May cause excessive hypotension. Monitor blood pressure closely. Indomethacin: May reduce the hypotensive effect of lisinopril. Monitor blood pressure closely. Lithium: May increase plasma lithium levels. Monitor lithium levels. Potassium-sparing diuretics, potassium supplements: May lead to hyperkalemia. Avoid use together. Monitor serum potassium levels.
2. **Drug-herb interactions:** Capsaicin: Increases risk of cough. Discourage use together.
3. **Drug-food interactions:** Potassium-containing salt substitutes: May lead to hyperkalemia.

Drug Interactions for Lisinopril

Drug	Interactions	Comments
Aliskiren	Increased risk of hypotension, syncope, hyperkalemia, and renal impairment (e.g., acute renal failure)	Monitor BP, renal function, and serum electrolytes closely. Concomitant use contraindicated in patients with diabetes mellitus; avoid concomitant use in patients with GFR <60 mL/minute per 1.73 m
Anti diabetic agents	Possible increased hypoglycemic effect, especially during initial weeks of combined treatment and in patients with renal impairment	
Diuretics	Increased hypotensive effect	If possible, discontinue diuretic before initiating lisinopril
Gold compounds (aurothioglucose, gold sodium thiomalate)	Rare nitritoid reactions (facial flushing, nausea, vomiting, hypotension)	
Lithium	Increased serum lithium concentrations; possible toxicity	
Potassium supplements or potassium-containing salt substitutes	Enhanced hyperkalemic effect	Use with caution; monitor serum potassium concentrations frequently
Propranolol	Clinically important interaction not observed	

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ADVERSE REACTIONS

CNS: Dizziness, headache, fatigue, paresthesia.
CV: Hypotension, orthostatic hypotension, chest pain.
EENT: Nasal congestion.
GI: Diarrhea, nausea, dyspepsia.
GU: Impotence.
Hematologic: Neutropenia, agranulocytopenia.
Metabolic: Hyperkalemia.
Respiratory: Dry, persistent, tickling, nonproductive cough; dyspnea.
Skin: Rashes on skin, urtecaria, alopecia,photo sensitivity, flushing
Others: Angioedema, Anaphylaxis.

CONTRAINDICATIONS[5]

Lisinopril is Contraindicated in patients hypersensitive to ACE inhibitors, in those with a history of angioedema related to previous treatment with ACE inhibitor, and in patients during the second and third trimesters of pregnancy.

Lisinopril is pregnancy category Class D due to its teratogenic effects (e.g., decreased fetal renal function, oligohydramnios, lung hypoplasia, skeletal malformations, death in the fetus/neonate, etc.), thus its use is contraindicated in pregnant women and/or fertile women without proper contraception. The amount secreted in breast milk and its effects in the breastfed infant is unknown, hence the use of lisinopril in breast feeding women is avoided.

No contraindications are known for patients with hepatic impairment. Lisinopril is cautiously used in patients at risk for hyperkalemia or in those with impaired renal function.
Lisinopril is not administered to patients suffering with angiodema. lisinopril is not administered within 36 hours before or after taking medicine that contains sacubitril (such as Entresto).

Special considerations

• lisinopril drug absorption is unaffected by food.
• To reduce the risk of hypotension, diuretics is discontinued 2 to 3 days before lisinopril therapy.
• If lisinopril doesn't adequately control blood pressure, diuretics may be added.
• Lower dosage is administered in patients with impaired renal function.
• Initiate drug therapy in the hospital for heart failure patients because of the risk of severe hypotension.
• Drug shouldn't be used after acute MI in patients at risk for severe hemodynamic deterioration or cardiogenic shock.
• Beneficial effects of lisinopril may require several weeks of therapy.

Breast-feeding patients

• cautiously use lisinopril in breast feeding women, because drug may appear in breast milk, but effect of drug
on infant is unknown.

Pediatric patients

• Safety and efficacy of drug in children haven't been established; use only if potential benefits outweigh risks.

Geriatric patients

• Because of impaired drug clearance geriatric patients may require lower doses.

TOXICITY:

Since lisinopril metabolism depends on renal excretion, overdose management consists of general supportive care, including gastric emptying strategies when appropriate, intravenous [IV] fluids, vasopressors, and hemodialysis. Maintenance of optimal blood pressure with fluids is critical in hypotensive patients.Some reports suggest the use of angiotensin II administration as an alternative supportive treatment for the treatment of ACE inhibitors overdose.

OVERDOSE

In one reported overdose, the half-life of lisinopril was prolonged to 14.9 hours. The case report of the event estimates that the individual consumed between 420 and 500 mg of lisinopril and survived. In cases of overdose of lisinopril, the drug can be removed by heamo dialysis.

Generic names of lisinopril

- Lisinopril (OS: BAN, DCF)
- L 154826 (IS)
- MK 521 (MerckSharpD) (IS)
- Lisinopril (PH: USP 41)
- Lisinopril (OS: USAN)
- Lisinopril Hydrate (OS: JAN)
- Lisinopril Dihydrate (PH: BP 2018)
- Lisinopril dihydrate (PH: Ph. Eur. 9)
- Lisinopril dihydraté (PH: Ph. Eur. 9)
- Lisinopril Hydrate (PH: JP XVII)
- Lisinopril-Dihydrat (PH: Ph. Eur. 9)
- Lisinoprilum dihydricum (PH: Ph. Eur.)

Marketed formulations of lisinopril

❖ **ZESTRIL (generic name Lisinopril)[6,7] :**

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Zestril is an ACE Inhibitor . It is used to treat the symptoms of high blood pressure and heart failure. It may be used alone or with other medications.
Zestril is supplied as 2.5 mg, 5 mg, 10 mg, 20 mg, 30 mg and 40 mg tablets for oral administration

Marketed **Zestril – 5mg tablet**

Dosage and administration of zestril

Hypertension

Initial Therapy of drug in adults: The recommended initial dose is 10 mg once a day. Dosage should be adjusted according to blood pressure response in patients. The usual dosage range of drug is 20 to 40 mg per day administered in a single daily dose.

Use With Diuretics In Adults:

If blood pressure is not controlled with Zestril , a low dose of a diuretic (e.g., hydrochlorothiazide, 12.5 mg)may be administered along with the drug. After the combination of diuretic with the drug, it may be possible to reduce the dose of Zestril. The recommended starting dose in adult patients with hypertension taking diuretics is 5 mg once per day.

Heart Failure: The starting dose for Zestril, when used with diuretics and (usually) digitalis as adjunctive therapy for systolic heart failure, is 5 mg once daily. The recommended starting dose of zestril in patients with hyponatremia (serum sodium < 130 mEq/L) is 2.5 mg once daily. The dose of the drug can be increased to a maximum of 40 mg once daily.

Adverse reactions: ZESTRIL has been generally found to be well tolerated in controlled clinical trials involving 1969 patients with hypertension or heart failure. For the most part, adverse experiences were mild and transient.

Storage conditions of ZESTRIL:

The drug is to be Stored at controlled room temperature, 20-25ºC (68-77ºF)[see USP]. It should be Protect from moisture, freezing and excessive heat. The drug need to be Dispense in air tight container. ZESTRIL is a trademark of the AstraZeneca group of companies. ©AstraZeneca 2008 Manufactured for: AstraZeneca Pharmaceuticals LP Wilmington, DE 19850 By: IPR Pharmaceuticals, Inc. Carolina, PR 00984.

❖ **Prinivil (generic name; prinivil)[8] :**

PRINIVIL contains lisinopril, a synthetic peptide derivative, and an oral, long-acting angiotensin converting enzyme[ACE] inhibitor.

PRINIVIL is supplied as 5 mg, 10 mg, and 20 mg tablets for oral administration. In addition to the active ingredient {lisinopril} of each tablet contains the following inactive ingredients: calcium phosphate, mannitol, magnesium stearate, and starch. The 10 mg and 20 mg tablets of prinvil also contain iron oxide.

Prinvil 20mg tablet

Indications

Hypertension

PRINIVIL is preferable for the treatment of hypertension in adult patients and pediatric patients 6 years of age and older to lower blood pressure. Lowering blood pressure lowers the risk of fatal and non-fatal cardiovascular events, and myocardial infarctions. These benefits have been seen in controlled trials of antihypertensive drugs from a wide variety of pharmacologic classes. PRINIVIL may be administered alone or with other antihypertensive agents..

Heart Failure

PRINIVIL is indicated to reduce signs and symptoms of heart failure in patients who are not responding adequately to diuretics and digitalis agents

Dosage and administration

Hypertension

Initial therapy of drug in adults: The recommended initial dose is 10 mg once a day. Adjust the dosage according to blood pressure response in patients. The usual dose of the drug ranges from 20 to 40 mg per day administered in a single daily dose.

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Heart Failure

The recommended starting dose of PRINIVIL, when used with diuretics and (usually) digitalis as adjunctive therapy is 5 mg once daily. The recommended starting dose of prinvil in patients suffering with hyponatremia (serum sodium <130 mEq/L) is 2.5 mg once daily. Increase as tolerated to a maximum of 40 mg once daily.

Storage

Store at controlled room temperature, 15-30°C (59-86°F), and protect from moisture. The drug is Dispensed in air tight container.

Methods of Estimation for Lisinopril [9,10] :

1) UV-visible spectroscopic methods 2) Spectrofluorimetric methods of estimation by reaction modifications 3) High performance liquid chromatographic methods 4) Combination of methods or techniques 5) Titrimetric methods 6) Miscellaneous methods

- **UV-visible spectroscopic method:**

UV spectrophotometric method have been developed which gives accurate result and gives quantitative estimation of the drug lisinopril in bulk and its marketed formulations by this method.

Figure 1 : Double beam UV Visible spectrophotometer

The drug Lisinopril shows absorption in UV-visible range in alkaline media produced by sodium hydroxide measured by absorption maxima method .

- **Spectrofluorimetric methods of estimation by reaction modifications:**

Lisinopril is non-fluorescent drug which is converted into fluorescent derivative. The Fluorimetric method is based upon the condensation reaction between primary amino group of Lisinopril and Fluorescien to form a fluorescent derivative (LSFN) in methanol at 60º C for 5 min. The resultant formation of fluorescent derivative can be determined by the UV (λmax 227 nm), NMR, Mass and IR spectra.

Lisinopril can be estimated by Spectrofluorimetric methods even in small quantities i.e in nanograms inn plasma or blood .The reported estimation of Lisinopril in pharmaceutical tablets using sequential injection analysis by spectrofluorimetric method based upon the reaction between Lisinopril and o-phthalaldhyde in presence of 2-mercaptoethanol (borate buffer medium, pH=10.6), calculated at excitation wavelength of 346 nm and emission at 455 nm

Figure 2 : Spectrofluorometer

- **High performance liquid chromatographic methods**

The determination of lisinopril have been widely used by HPLC methods . As HPLC method gives simple, accurate results . HPLC of lisinopril in dosage forms in addition to spiked human plasma by using solid phase extraction was carried out by spectrophotometry and reversed-phase HPLC.

HPLC method is suitable for quantitative determination of the drugs was proved by validation in accordance with International Conference on Harmonization (ICH) guidelines. This method is precise and accurate and can be used for analysis of pharmaceutical preparations in quality control (QC) and clinical laboratories.

Arayne et al. developed HPLC method for simultaneous determination of Metformin and ACE inhibitors like lisinopril, captopril, etc and its degradable product in bulk drugs, pharmaceutical products and in human serum. At 218 nm analytes peaks were observed. The HPLC method was successfully applied to quantitate metformin, lisinopril, captopril, and enalapril in pharmaceutical formulations and human serum

In this study, a quantitative determination of lisinopril in human serum was developed which is a sensitive, specific, precise and accurate method and validated. The mean recovery of lisinopril from

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 2 Mar-Apr 2021, pp: 600-607 www.ijprajournal.com ISSN: 2249-7781

serum samples was 88%. The LOQ for lisinopril was 6 ng/ml

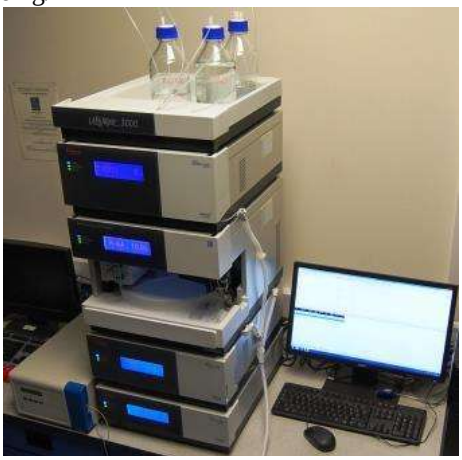

Figure 3: HPLC- High performance liquid chromatography

- **Titrimetric methods :**

For the analysis of Lisinopril, different titrimetric methods is carried out in which include following: In the middle of 18 century there was origin of titrimetric method of analysis. Gay–Lussac in 1835 invented the volumetric methods which actually lead to the foundation of the term titration. While the assay method is very old yet but certain signs of some renovation may including as dispersion to non-aqueous titrations, intensifying the field of application to weak acids and bases as well as to detection of potentiometric end point improving the accuracy of the methods. Simultaneously detection of group analysis procedures, in which titrimetric methods play a vital role in establish reaction rates.

Titrimetric methods have been used for the determination of lisinopril 1 in commercial dosage forms.

Titrimetric methods have widely been used for drug estimation and for the estimation of degradation products of the pharmaceuticals.

Patents of lisinopril:

- **Monohydrate lisinopril [11]**

The present invention relates to a novel monohydrate form of 1-(N^2-[(S)-1-carboxy-3-phenylpropyl]-L-lysyl)-L-proline. 1-(N^2-[(S)-1-carboxy-3-phenylpropyl]-L-lysyl)-L-proline is known under the generic name lisinopril . Its novel monohydrate form is referred to as monohydrate lisinopril form

Their invention relates to the use of monohydrate lisinopril form in medical treatments, pharmaceutical compositions comprising monohydrate lisinopril form in particular 'fast melt' formulations, and processes for the preparation of monohydrate lisinopril. " Moreover, from the invention it has been found that monohydrate lisinopril form possess far greater solubility than lisinopril dehydrate.

The monohydrate lisinopril form is more suitable to certain formulations where quick solubility is desired, such as 'fast melt' (melt-on-the-tongue type) formulations as it is proven to have more solubility.

This invention also provides the use of monohydrate lisinopril form in treating hypertension, congestive heart failure, acute myocardial infarction and in renal and retinal complications of diabetes mellitus.

Patent citations:

Publication number	Priority date	Publication date	Assignee	Title
WO2000069417A1	*1999-05-14	2000-11-23	Eli Lilly And Company	Process for preparing pharmaceutical bulk material having uniform dissolution

- **Lisinopril compositions having large-particle DCPD[dibasic calcium phosphate dehydrate [12]**

The present invention relates to a pharmaceutical composition comprising lisinopril and (DCPD), which is produced by a process comprising by mixing lisinopril and DCPD with a specific surface area of less than 1.5 m^2g^{-1}. The use of this large particle sized DCPD in a lisinopril formulation/composition has the effect of reducing the amount of the lisinopril degradation product DKP that is formed, thereby increasing the shelf-life of tablets formulated with the larger sized DCPD, particularly those with of low doses of lisinopril.

Priority Applications

Application	Priority date	Filing date	Title
US09/962,429	2001-09-24	2001-09-24	Lisinopril compositions having large-particle DCPD

- **Rapid Determination of Lisinopril Level in Human Plasma by LC-MS/MS[13]**

A rapid liquid chromatographic mass spectrometry (LC-MS/MS) assay to measure lisinopril level in

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Volume 6, Issue 2 Mar-Apr 2021, pp: 600-607 www.ijprajournal.com ISSN: 2249-7781

human plasma was developed and validated as per the study. 1.0 ml plasma samples containing lisinopril and 0.1 µg ramipril (as internal standard, IS) were extracted with 4 ml tert-butyl methyl ether and reconstituted in 60 µl mobile phase (5 mM ammonium formate and acetonitrile; 30:70, v:v). . Retention time of lisinopril and the IS was 1.28 and 1.86 minutes, respectively

The limit of detection of lisinopril in plasma was 0.5 ng/ml Lisinopril stability in processed (24 hours at room temperature or 48 hours at -20°C) and the unprocessed samples (24 hours at room temperature, 12 weeks at -20°C, or three freeze-thaw cycles) was found to be ≥92% from their study.

- **Elementary OsmoticTablet Of Lisinopril Dihydrate [14]**

Elementary osmotic tablets of Lisinopril Dihydrate were developed using Sodium chloride as a key ingredient which gives osmogent property which provides driving force inside the core tablet and which leads to release of the drug. Microcrystalline cellulose[mcc] used as a release retardant material in the present work.

Different types of formulations were prepared by varying the concentrations using 3^2 factorial designs. It was applied to see the effect of variables Sodium chloride (X1) and MCC (X2) on the response percentage drug release as a dependent variable. These formulations were evaluated for determination of , Hardness, Flow property, Thickness, Friability, Drug content and In vitro drug release. The prepared Tablets were coated with a semipermeable membrane using 5% w/v cellulose acetate(CA) in acetone and PEG 400(1%) used as Plasticizer. Coated Elementary osmotic tablets were drilled for delivery orifice using a standard micro drill of diameter size 0.8 mm. the drug release rate was directly proportional to delivery orifice size. The optimized formulation was stable for 3 mo of accelerated stability study.

Thus from the results of their study clearly indicated that developed osmotically controlled release tablet of Lisinopril Dihydrate provide release of drug at a predetermined rate and for a predetermined time in a controlled manner.

- **Formulation and Evaluation of Lisinopril Dihydrate Transdermal Proniosomal Gels [15]:**

In their study transdermal Lisinopril proniosomal gels was formulated by using Lecithin, Cholesterol as encapsulating agents, Surfactant, Span and permeation enhancers. The study methodology encompasses compatibility studies using FTIR spectra, evaluation of proniosomal gels for pH determination, Viscosity, Vesicle size analysis, rate of spontaneity, encapsulation efficiency, in vitro skin permeation studies and stability studies. The proniosomes showed spherical and homogenous structure in optical microscopy.

All prepared formulations showed zero order drug release by diffusion mechanism. The stability studies showed that proniosomal gels were stable at 4 to 80C and 25±20C. The results indicated that the proniosomal gels of could be formulated for controlled release of Lisinopril. The prepared proniosomal gels are suitable for Lisinopril once a day controlled release formulation.

II. CONCLUSION:

Lisinopril is indicated in treatment of essential hypertension and in renovascular hypertension. It has narrow absorption window with only 25% of the drug being absorbed in the GIT. Lisinopril increases caridacOutput and it decreases the pulmonary capillary wedge pressure and mean arterial pressure in patients with congestive heart failure. Lisinopril has been available for three decades and is a relatively safe medication for hypertension. It is usually administered by the primary care physicians, nurse practitioner, emergency department physicians and cardiologist. Lisinopril is generally well tolerated by patients with heart failure. lisinopril is as least effective and well tolerated as other members of ACE inhibitor class for the treatment of congestive heart failure.

REFERENCES

[1]. Lisinopril drugs.com retrived 23 December 2018
[2]. Lisinopril". PubChem Retrieved 6 June 2018..
[3]. Mayur Parmar; Venkata Satish Pendela et al Ncbi dec2,2020 lisinopril
[4]. Bjorn,beermann, M.D.,PHD Pharmacokinetics of lisinopril volume85, issue3,supplement2,25-30september23,1988 The American journal of medicine.
[5]. N J Warner et al Safety profiles of the angiotensin-converting enzyme inhibitors national center for biotechnology information pubmed drugs 1988;35 Suppl

5:89-97. doi: 10.2165/00003495-198800355-00016.

[6]. Zestril FDA[food and drug administration]5. Federico et al Journal of Cardiovascular Pharmacology: 1987-ps27-s34 the clinical pharmacology of lisinopril.

[7]. "Zestril- lisinopril tablet". DailyMed. 31 October 2019. Retrieved 5 August 2020.

[8]. prinvil-lisinopril tablet US national library of medicine merck sharp and dohme corp

[9]. Methods of Analysis of Lisinopril: A Review Journal of Bioequivalence & Bioavailability Wajiha Gul, Zarnab Augustine et al Dow University of Health Sciences, Dow College of Pharmacy, Karachi, Pakistan Faculty of Pharmacy, Jinnah University for Women.

[10]. Analytical Determination of Lisinopril Using UV Spectrophotometer and HPLC: An Overview Safila Naveed Faculty of Pharmacy Jinnah University for Women, Pakistan Modern Chemistry & Applications

[11]. John brown Astrazeneca AB 2001, 2002 monohydrate lisinopril US 6465615B1 patent

[12]. Ronald John Roberts David Brandon Bowen Syngenta Ltd AstraZeneca AB 2001, 2002 Lisinopril compositions having large-particle DCPD patent.

[13]. 1990 Feb 24;335(8687):487-8. doi: 10.1016/0140-6736(90)90731-j. Rapid Determination of Lisinopril Level in Human Plasma by LC-MS/MS Rajaa F Hussein, Syed N Alvi, and Muhammad M Hammami* Clinical Studies and Empirical Ethics Department, King Faisal Specialist Hospital and Research Center, Saudi Arabia Published on : August 02, 2019.

[14]. Bhushan A bhairav et al Department of Quality Assurance Techniques; R. G. Sapkal College of Pharmacy, Anjaneri, Nashik 422213, Maharashtra international journal of current pharmaceutical research IJCPR 22 july 2017

[15]. Shamsheer ahmed, sudheer B et al Formulation and Evaluation of Lisinopril Dihydrate Transdermal Proniosomal Gels JAPS journal of applied pharmaceutical science **Volume : 1 Issue :** 8, October 2011

[16]. Analytical Determination of Lisinopril Using UV Spectrophotometer and HPLC: An Overview Safila Naveed Faculty of Pharmacy Jinnah University for Women, Pakistan Modern Chemistry & Applications

[17]. Federico et al Journal of Cardiovascular Pharmacology: 1987-ps27-s34 the clinical pharmacology of lisinopril

[18]. Lisinopril monograph for professionals drugs.com American society of health-systempharmacists. Retrived 23 december 2018