

# Survey Based Report on Widely Prescribed Enalapril Drug for Treatment of Hypertension

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**Abstract:** Enalapril maleate is an orally active angiotensin-converting enzyme inhibitor. It lowers peripheral vascular resistance without causing an increase in heart rate. Enalapril 10 to 40 mg/day administered either once or twice daily is effective in lowering blood pressure in all grades of essential and reno vascular hypertension, and shows similar efficacy to usual therapeutic dosages of hydrochlorothiazide, beta-blockers (propranolol, atenolol and metoprolol) and captopril. Most patients achieve adequate blood pressure control on enalapril alone or with hydrochlorothiazide. In patients with severe congestive heart failure resistant to conventional therapy, enalapril improves cardiac performance by a reduction in both preload and afterload, and improves clinical status long term. Enalapril appears to be well tolerated, with few serious adverse effects being reported. It does not induce the bradycardia associated with beta-blockers or the adverse effects of diuretics on some laboratory values. In fact, the hypokalemic effect of hydrochlorothiazide is attenuated by the addition of enalapril. The incidence of the main (but rare) side effects of hypotension in hypovolemic patients and reduced renal function in certain patients with reno vascular hypertension, which are also seen with captopril, might be reduced by careful dosage titration, discontinuation of diuretics, and monitoring of at-risk patients. Thus, enalapril is a particularly worthwhile addition to the antihypertensive armamentarium, as an alternative for treatment of all grades of essential and reno vascular hypertension. It also shows promise in the treatment of congestive heart failure.

**Keywords:** Enalpril, Hypertension And Antihypertensive Drugs.

## I. INTRODUCTION

### Definition Of Hypertension :

Hypertension is defined as an abnormal elevation in diastolic pressure and/or systolic pressure; mean arterial pressure is also elevated in hypertension, but it is not usually measured in people. In past years, the diastolic value was emphasized in assessing hypertension. However, elevations in systolic pressure ("systolic hypertension") are also associated with increased incidence of coronary and cerebrovascular disease (e.g., stroke). Therefore, we now recognize that both systolic and diastolic pressure values are important to note. According to the latest u.s.

National guideline [5], the following represents different stages of hypertension :

Classification	Systolic (Mmhg)	Diastolic (Mmhg)
Normal	<120	<80
Pre-Hypertension	120-139	80-89
Stage 1	140-159	90-99
Stage 2	>160	

### Symptoms Of High Blood Pressure

Although patients with isolated hypertension are usually asymptomatic, occasionally they have symptoms such as dizziness, headache (especially pulsating headaches behind the eyes that occur early in the morning), blurred vision, facial flushing or tinnitus (ringing sound in the ears).hypertension which is very severe with a systolic blood pressure (sbp) >240 mmhg or diastolic blood pressure (dbp) >120 mmhg is called accelerated hypertension.

Accelerated hypertension is associated with confusion, visual disturbances, nausea and vomiting. When hypertension causes increased intracranial pressure (pressure exerted by the cranium on the brain tissue and brain fluid), it is called malignant hypertension or hypertensive crisis and is a medical emergency that requires immediate reduction of the blood pressure. This condition may present with end-organ damage.

Over time, untreated high blood pressure can damage organs such as the heart, kidneys or eyes leading to complications such as: angina, heart attack or heart failure, stroke, kidney failure, peripheral arterial disease, retinopathy (eye damage) .

### Types Of High Blood Pressure :

There are two main types of high blood pressure:

#### (A) Essential (primary) Hypertension

1. The main form of high blood pressure – accounts for around 90–95% of cases
2. Has no single identifiable cause
3. Potential causes include genetic and environmental factor

#### (B) Secondary Hypertension

1. Rare forms of high blood pressure
2. Caused by another medical condition or treatment
3. Causes include kidney problems (renovascular hypertension), adrenal gland tumors, thyroid disease, and narrowing of the aorta (the main artery that takes blood from the heart to the rest of the body)
4. Other types of high blood pressure include :
5. Isolated systolic hypertension – the systolic pressure ( top number ) is raised but the diastolic pressure is normal
6. Isolated diastolic hypertension – the diastolic pressure (bottom number) is raised but the systolic pressure is normal.
7. White coat hypertension – where the blood pressure is raised due to the stress of a visit to the doctor or nurse .

### Pathophysiology

#### Objectives :

1. Understand the hemodynamic determinants of systemic hypertension.
2. Recognize primary and secondary forms of hypertension.
3. Understand the role of the kidney in systemic hypertension: innocent bystander or instigator.
4. Recognize the role of angiotensin ii, aldosterone, and the sympathet .

Hypertension is a chronic elevation of blood pressure that, in the long-term, causes end-organ damage and results in increased morbidity and mortality. Blood pressure is the product of cardiac output and systemic vascular resistance vascular tone may be elevated because of increased  $\alpha$ adrenoceptor stimulation or increased release of peptides such as angiotensin or endothelins. The final pathway is an increase in cytosolic calcium in vascular smooth muscle causing vasoconstriction. Several growth factors, including angiotensin and endothelins, because an increase in vascular smooth muscle mass termed vascular remodeling with ageing, stiffening of the aorta and elastic arteries increases the pulse pressure. The autonomic nervous system plays an important role in the control of blood pressure. In hypertensive patients, both increased release of, and enhanced peripheral sensitivity to, norepinephrine can be found. In addition, there is increased responsiveness to stressful stimuli. Another feature of arterial hypertension is a resetting of the baroreflexes and decreased baroreceptor sensitivity. The renin–angiotensin system is involved at least in some forms of hypertension (e.g. Renovascular hypertension) and is suppressed in the presence of primary hyperaldosteronism. Elderly or black patients tend to have low-renin hypertension.

### Diagnosis :

Hypertension is diagnosed on the basis of a persistently high blood pressure. Traditionally, this requires three separate sphygmomanometer measurements at one monthly interval. Initial assessment of the hypertensive people

should include a complete history and physical examination. With the availability of 24-hour ambulatory blood pressure monitors and home blood pressure machines, the importance of not wrongly diagnosing those who have white coat hypertension has led to a change in protocols. In the united kingdom, current best practice is to follow up a single raised clinic reading with ambulatory measurement, or less ideally with home blood pressure monitoring over the course of 7 days.

### Equipment

1. Cuff size: The bladder size (six sizes are available) should encircle at least 80% of the arm circumference and cover two thirds of the arm length; if not, place the bladder over the brachial artery. If bladder is too small, spuriously high readings may result. The lower edge of the bladder should be within 2.5 cm of the Antecubital fossa .
2. Manometer: Mercury, Aneroid or Electronic devices used in measurement of blood pressure should be calibrated frequently and routinely against standards (typically every 6 months) to assure accuracy. Ensure that the equipment used is in working order: clean, calibrated, filled with non-leaking tubing and has a properly sized cuff.
3. ECG (nazzareno galie et al, 2004, european society of cardiology) :The ECG may provide suggestive or supportive evidence of hypertension by demonstrating right ventricular hypertrophy and strain, and right atrial dilation. Right ventricular hypertrophy on ECG is present in 87% and right axis deviation in 79% of patients with hypertension. However, the ECG has inadequate sensitivity (55%) and specificity (70%) to be a screening tool for detecting significant hypertension. A normal ECG does not exclude the presence of severe PH.
4. Chest Radiograph :In 90% of IPAH patients the chest radiograph is abnormal at the time of diagnosis. Findings include central pulmonary arterial dilatation which contrasts with 'Pruning' (loss) of the peripheral blood vessels. Right Atrial and Ventricular enlargement may be seen and it progresses in more advanced cases. The chest radiograph allows associated moderate-to-severe lung disease or pulmonary venous hypertension due to left heart abnormalities to be reasonably excluded. However, a normal chest radiograph does not exclude mild post capillary pulmonary hypertension including left-heart disease or pulmonary veno-occlusive disease.
5. Transthoracic Doppler-Echocardiography : Transthoracic Doppler-Echocardiography (TTE) is an excellent non-invasive screening test for the patient with suspected pulmonary hypertension. TTE estimates pulmonary artery systolic pressure (PASP) and can provide additional information about the cause and consequences of ph. Pasp is equivalent to right ventricular systolic pressure (RVSP) in the absence of pulmonary outflow obstruction. RVSP is estimated by measurement of the systolic regurgitant tricuspid flow velocity V and an estimate of right atrial pressure (RAP) applied in the formula:  $RVSP = 4v^2 + RAP$ . RAP is either a standardised value, or estimated value from characteristics of the inferior vena cava<sup>51</sup> or from jugular venous distension. Tricuspid regurgitant jets can be assessed in the majority (74%) of patients with PH.<sup>52</sup> most studies report a high correlation (0.57–0.93) between TTE and Right Heart Catheterization (RHC) measurements of PASP.<sup>53</sup> However, in order to minimise false positives. It is important to identify specific values for the definition of PH as assessed by TTE.

### Complementary and alternative treatment for hypertension :

There are many types of complementary and alternative treatments believed to be effective for treating hypertension. Get the facts on your options.

#### High blood pressure drugs :

Your doctor has hundreds of different high blood pressure drugs to choose from. These medications work in a variety of ways to lower blood pressure.

#### Calcium channel blockers :

Calcium channel blockers are drugs used to lower blood pressure. They work by slowing the movement of calcium into the cells of the heart and blood vessel walls, which makes it easier for the heart to pump and widens blood vessels .

**ACE inhibitors :**

Angiotensin converting enzyme (ACE) inhibitors are high blood pressure drugs that widen or dilate your blood vessels to improve the amount of blood your heart pumps and lower blood pressure.

**Diuretics (water pills) :**

For high blood pressure, diuretics, commonly known as “water pills,salt through the urine. Getting rid of excess salt and fluid helps lower blood pressure and can make it easier for your heart to pump. 5)Beta-blockers :

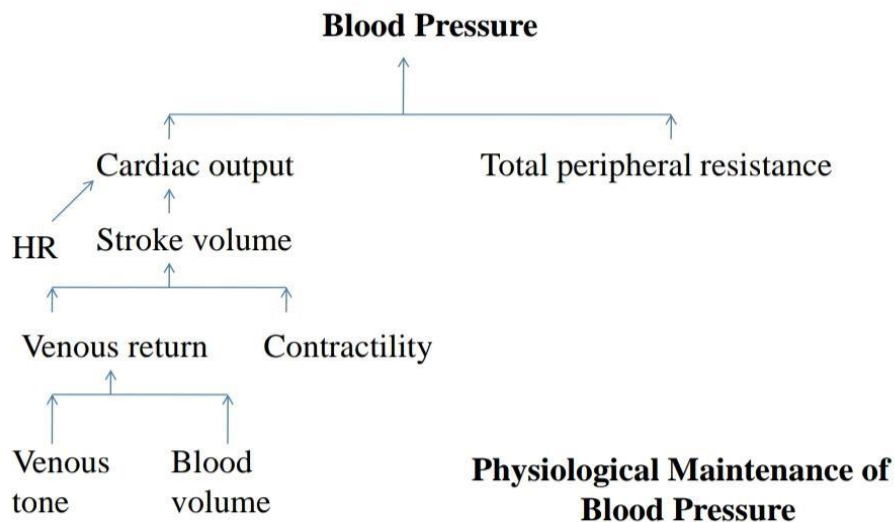
Beta-blockers are drugs used to treat high blood pressure. They block the effects of the sympathetic nervous system on the heart.

**Care for high blood pressure :**

- The most important element in managing high blood pressure is follow-up care. Here are six tips to keep in mind about follow-up care .
- Hypertension management: In-home blood pressure monitoring .
- Monitoring your own blood pressure is a good way to keep on top of hypertension. Get tips on how to prepare, and step-by-step instructions for taking your own blood pressure readings.
- High blood pressure medication guidelines: What you want to know if your doctor has prescribed medication to lower your blood pressure, here are twelve things to keep in mind about your treatment protocol.

**Antihypertensive drugs**

Definition: According to who hypertension is persistent increase in blood pressure i.e 140 mmhg systolic and 90mm hg diastolic.



Classification of Antihypertensive drugs :

**1) Diuretics**

Thiazides: Hydrochlorothazide, Chlorthalidone, Indapamide High ceiling: furosemide, etc.  
K+ sparing: spironolactone, amiloride

**2) ACE inhibitors**

Eg. Captopril, enalapril, lisinopril, ramipril, fosinopril, etc.

**3) Angiotensin (AT 1 receptor) blockers**

Eg. Losartan, candesartan, valsartan, telmisartan, etc.

**4) Direct Renin inhibitor**

Eg. Aliskiren

**5) Calcium Channel blockers**

Eg. Verapamil, Diltiazem, Nifedipine, Amlodipine etc.

**6)  $\beta$ - Adrenergic blockers**

Eg. Propranolol, Metoprolol, Atenolol, etc.

B+ $\alpha$  Adrenergic blockers

Eg. Labetalol, Carvedilol

A- Adrenergic blockers

Eg. Prazosin, terazosin, doxazosin

Central sympatholytics

Eg. Clonidine, methyldopa, phenoxybenzamine

Vasodilators

Eg. Arteriolar: hydralazine, minoxidil, diazoxide

Arteriolar +venous: sodium nitroprusside Enalapril :

Defination – Enalapril is a medication used in the management of hypertension and congestive heart failure. It is an angiotensin-converting enzyme inhibitor. This activity outlines the indications, action, and contraindications for enalapril as a valuable agent in managing hypertension and other disorders. This activity will highlight the mechanism of action, adverse event profile, and other key factors (e.g., off-label uses, dosing, pharmacodynamics, pharmacokinetics, monitoring, relevant interactions) pertinent for members of the healthcare team in the care of patients with hypertension and related conditions.

**Mechanism of action :**

Chemically Enalapril is (s)-1-[n-[1-(ethoxycarbonyl)-3-phenylpropyl]-l-alanyl]-l-proline. The active form of enalapril is enalaprilat. It inhibits angiotensin-converting enzyme (ace), thereby reducing the level of angiotensin-ii. This action causes a decrease in total peripheral resistance without an increase in cardiac oxygen demand. There is a decrease in Aldosterone and an increase in serum renin levels .

**Pharmacokinetics :**

- 1.Absorption: good oral absorption .
- 2.Distribution: volume of distribution is 1 to 2.4 l/kg .
- 3.Metabolism: de-esterified into enalaprilat in the liver .
- 4.Excretion: excreted into the bile and urine .

**Administration :**

Food does not affect the absorption and metabolism of enalapril; therefore, administration can be irrespective of food intake. The oral solution is available in 1 mg/ml concentration, and tablets are available in 2.5 mg, 5 mg, 10 mg, or 20 mg strength. Typical adult dosing regimens are once or twice daily, depending on the indication.

**Adverse effects :**

- 1.The side effect most commonly encountered with ace inhibitors is cough. The cough is characteristically non-productive and stops with the discontinuation of the drug.
- 2.Other adverse effects of enalapril are hypotension, hyperkalemia, angioedema, cholestatic jaundice, and hypersensitivity reaction.
- 3.Vasodilation caused by enalapril to reduce the afterload of the heart and decrease the total peripheral resistance is also responsible for hypotension. At first, the patient may only complain of a feeling of light-headedness on standing (orthostatic hypotension), which may later progress to fainting spells.

**Monitoring :**

Monitoring the vital signs, renal function, and cardiac activity is of the utmost importance when administering enalapril in patients with relative contraindications. The clinician should consider the following tests:

1. Renal function
2. Serum potassium
3. Serum creatinine
4. Bun
5. Complete blood count
6. Sgot and sgpt (hepatic transaminases)

**Toxicity :**

The occurrence of enalapril toxicity is rare. A single such case of toxicity came into light in 1984 when a woman tried to commit suicide by ingesting 300 mg of enalapril (a hundred times the normal dose) and 225 mg oxazepam. In 1986, another woman tried the same by ingesting 440 mg of enalapril with 42 mg warfarin. Fortunately, both recovered from acute intoxication of enalapril. Fluid resuscitation played a major role in increasing intravascular volume as hypotension was the major complication. The second patient died forty days later due to intractable heart failure. Hence enalapril toxicity can be managed by giving symptomatic treatment. Enalaprilat is removed from neonatal circulation by peritoneal dialysis and can be removed from general circulation via hemodialysis.

**II. MATERIAL AND METHODOLOGY**

**Study design**

This real world, retrospective multicentric, observational analysis was conducted manipal healthcare centers in banner and survey based study at chikhali utilizing medical records of adult patients with hypertension who had received treatment with enalapril data were collected retrospectively from medical records of eligible patients <including demographic characteristics , duration of disease , co-morbidities, concomitant medication, and dosage pattern from selected medical and hospital.

**Result:**

The most often prescribed medication was enalapril and captopril .among which enalapril is widely prescribed because, when compared with captopril, enalapril have is more potent, longer acting and possibly safer with fewer side effect. Enalapril relaxes the blood vessels. This lowers blood pressure and increases the supply of blood and oxygen to the heart. Enalapril is also used in combination with other medicines to treat congestive heart failure and cut down on the number of hospital visits for heart problems .

**Discussion:**

At the chikhali area , we have a survey at about fifty medical supply stores. When antihypertensive medications were surveyed, we discovered that the most often prescribed medication was enalapril and captopril .among which enalapril is widely prescribed because, when compared with captopril, enalapril have is more potent, longer acting and possibly safer with fewer side effect.

Apart from which we also visited manipal hospital to have a survey on most commonly prescribed antihypertensive drugs. We have discussed with cardiologist and nephrologist specialist that why enalapril is widely prescribed in hypertension as compared with captopril . The discussion comes with the end that enalapril is more potent, longer acting and possibly safer with fewer side effect.

**III. CONCLUSION**

Enalapril is a medication used in the management of hypertension and congestive heart failure. It is an angiotensin-converting enzyme inhibitor. This activity outlines the indications, action, and contraindications for enalapril as a valuable agent in managing hypertension and other disorders. This activity will highlight the mechanism of action, adverse event profile, and other key factors (e.g., off-label uses, dosing, pharmacodynamics, pharmacokinetics,



monitoring, relevant interactions) pertinent for members of the healthcare team in the care of patients with hypertension and related conditions.

Like captopril, enalapril selectively suppresses the rennin–angiotensin–aldosterone system, inhibits angiotensin-converting enzyme, and prevents conversion of angiotensin I into angiotensin II. It is used for hypertension and chronic cardiac insufficiency.

#### REFERENCES

- [1]. Abe K, Ito T, Sato M, Haruyama T, Sato K, Omata K, Hiwatari M, Sakurai Y, Imai Y, Yoshinaga K. Role of prostaglandin in the antihypertensive mechanism of captopril in low renin hypertension. *Clin Sci (Lond)* 1980 Dec;59 (Suppl 6):141s–144s.
- [2]. Biollaz J, Burnier M, Turini GA, Brunner DB, Porchet M, Gomez HJ, Jones KH, Ferber F, Abrams WB, Gavras H, et al. Three new long-acting converting-enzyme inhibitors: relationship between plasma converting-enzyme activity and response to angiotensin I. *Clin Pharmacol Ther.* May;29(5):665–670.
- [3]. Biollaz J, Brunner HR, Gavras I, Waeber B, Gavras H. Antihypertensive therapy with MK 421: angiotensin II—renin relationships to evaluate efficacy of converting enzyme blockade. *J Cardiovasc Pharmacol.* 1982 Nov-Dec;4(6):966–972.
- [4]. Biollaz J, Schelling JL, Jacot Des Combes B, Brunner DB, Desponds G, Brunner HR, Ulm EH, Hichens M, Gomez HJ. Enalapril maleate and a lysine analogue (MK-521) in normal volunteers; relationship between plasma drug levels and the renin angiotensin system. *Br J Clin Pharmacol.* Sep;14(3):363–368.
- [5]. Brunner DB, Desponds G, Biollaz J, Keller I, Ferber F, Gavras H, Brunner HR, Schelling JL. Effect of a new angiotensin converting enzyme inhibitor MK 421 and its lysine analogue on the components of the renin system in healthy subjects. *Br J Clin Pharmacol.* 1981 May;11(5):461–467.
- [6]. Brunner HR, Waeber B, Nussberger J, Schaller MD, Gomez HJ. Long-term clinical experience with enalapril in essential hypertension. *J Hypertens Suppl.* 1983 Oct;1(1):103–107.
- [7]. Case DB, Atlas SA, Laragh JH, Sullivan PA, Sealey JE. Use of first-dose response or plasma renin activity to predict the long-term effect of captopril: identification of triphasic pattern of blood pressure response. *J Cardiovasc Pharmacol.* 1980 Jul-Aug;2(4):339–346.
- [8]. Chrysant SG, Brown RD, Kem DC, Brown JL. Antihypertensive and metabolic effects of a new converting enzyme inhibitor, enalapril. *Clin Pharmacol Ther.* 1983 Jun;33(6):741–746. 9)Cody RJ, Covit AB, Schaer GL, Laragh JH. Evaluation of a long-acting converting enzyme inhibitor (enalapril) for the treatment of chronic congestive heart failure. *J Am Coll Cardiol.* 1983 Apr;1(4):1154–1159.
- [9]. Cody RJ, Laragh JH, Atlas SA, Case DB. Converting enzyme inhibition to identify and treat renin-mediated or sodium-volume related forms of increased peripheral resistance in hypertension and in congestive heart failure. *J Hypertens Suppl.* 1983 Oct;1(1):77–84. 11)De Leeuw PW, Hoogma RP, van Soest GA, Tchang PT, Birkenhäger WH. Humoral and renal effects of MK-421 (enalapril) in hypertensive subjects. *J Cardiovasc Pharmacol.* 1983 SepOct;5(5):731–736.
- [10]. DiCarlo L, Chatterjee K, Parmley WW, Swedberg K, Atherton B, Curran D, Cucci M. Enalapril: a new angiotensin-converting enzyme inhibitor in chronic heart failure: acute and chronic hemodynamic evaluations. *J Am Coll Cardiol.*
- [11]. Dunkman WB, Wilen M, Franciosa JA. Enalapril (MK-421), a new angiotensin-converting enzyme inhibitor. Acute and chronic effects in heart failure. *Chest.* 1983 Nov;84(5):539–545.
- [12]. Dunn FG, Oigman W, Ventura HO, Messerli FH, Kobrin I, Frohlich ED. Enalapril improves systemic and renal hemodynamics and allows regression of left ventricular mass in essential hypertension. *Am J Cardiol.* 1984 Jan 1;53(1):105–108.
- [13]. Ferguson RK, Vlasses PH, Swanson BN, Mojaverian P, Hichens M, Irvin JD, Huber PB. Effects of enalapril, a new converting enzyme inhibitor, in hypertension. *Clin Pharmacol Ther.* 1982 Jul;32(1):48–53.
- [14]. Fitzpatrick D, Nicholls MG, Ikram H, Espiner EA. Haemodynamic, hormonal, and electrolyte effects of enalapril in heart failure. *Br Heart J.* 1983 Aug;50(2):163–169.

- [15]. Fouad FM, Tarazi RC, Bravo EL. Cardiac and haemodynamic effects of enalapril. *J Hypertens Suppl.* 1983 Oct;1(1):135–142.
- [16]. Gavras H, Biollaz J, Waeber B, Brunner HR, Gavras I, Davies RO. Antihypertensive effect of the new oral angiotensin converting enzyme inhibitor “MK-421”. *Lancet.* 1981 Sep 12;2(8246):543–547.
- [17]. Gomez HJ, Cirillo VJ, Jones KH. The clinical pharmacology of enalapril. *J Hypertens Suppl.* 1983 Oct;1(1):65–70.
- [18]. Griffing GT, Melby JC. The therapeutic use of a new potassium-sparing diuretic, amiloride, and a converting enzyme inhibitor, MK-421, in preventing hypokalemia associated with primary and secondary hyperaldosteronism. *Clin Exp Hypertens A.* 1983;5(6):779–801.
- [19]. Griffing GT, Sindler BH, Aurecchia SA, Melby JC. Temporal enhancement of reninaldosterone blockade by enalapril, an angiotensin-converting enzyme inhibitor. *Clin Pharmacol Ther.* 1982 Nov;32(5):592–598.
- [20]. Griffing GT, Sindler BH, Aurecchia SA, Melby JC. Reversal of diuretic-induced secondary hyperaldosteronism and hypokalemia by enalapril (MK-421): a new angiotensin-converting enzyme inhibitor. *Metabolism.* 1983 Jul;32(7):711–716.
- [21]. Griffing GT, Wilson TE, Melby JC. Altered fractional tetrahydroaldosterone excretion during pharmacological blockade and activation of the renin-aldosterone system. *J Clin Endocrinol Metab.* 1982 Dec;55(6):1217–1221.
- [22]. Gross DM, Sweet CS, Ulm EH, Backlund EP, Morris AA, Weitz D, Bohn DL, Wenger HC, Vassil TC, Stone CA. Effect of N-[(S)-1-carboxy-3-phenylpropyl]-L-Ala-L-Pro and its ethyl ester (MK-421) on angiotensin converting enzyme in vitro and angiotensin I pressor responses in vivo. *J Pharmacol Exp Ther.* 1981 Mar;216(3):552–557.
- [23]. Hodsman GP, Brown JJ, Cumming AM, Davies DL, East BW, Lever AF, Morton JJ, Murray GD, Robertson I, Robertson JI. Enalapril in the treatment of hypertension with renal artery stenosis. *Br Med J (Clin Res Ed)* 1983 Nov 12;287(6403):1413–1417.