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A REVIEW ON DELIVERY OF ANTIHYPERTENSIVE DRUGS THROUGH SUBLINGUAL ROUTE

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ABSTRACT: Hypertension is a major risk factor in the development of cardiovascular diseases and has emerged as one of the largest death causing diseases for mankind. There are number of medicines useful for treatment of high blood pressure but the main obstacle for the oral delivery of antihypertensive drugs is low bioavailability due to first pass metabolism. Also, if there is sudden increase in blood pressure, rapid onset of pharmacological action becomes necessary to enable the patients to resume their functional activities. The drug absorbed via sublingual blood vessels bypasses the hepatic first pass metabolism processes giving acceptable bioavailability with low doses and hence decreases the side effects. As sublingual area is more permeable than cheeks and palatal area of mouth, delivery by this route leads to rapid onset of action of drug. It is also convenient for patients having difficulty in swallowing. The present article gives a brief view on various research studies undertaken in the areas of sublingual delivery of antihypertensive drugs to improve the bioavailability and patient compliance.

INTRODUCTION: Hypertension, a major risk factor in the development of cardiovascular diseases (CVD) is a leading cause of death worldwide. Hypertension is common in both developed and low and middle income countries.[1] The achievement of desired blood pressure targets has become a challenge to reduce the risk of morbidity and mortality. As the patients with sudden increase in blood pressure and acute angina attack have marked reduced functional ability and extreme restlessness, in such cases rapid onset of pharmacological action is of prime importance so that patients could return to normal state and resume their functional activities.

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This can effectively be achieved by parenteral administration, but this method may not always be convenient for patients. Therefore, there is growing interest in developing non-parenteral, reliable and convenient dosage forms using administrative routes where a rapidly dissolved drug is immediately absorbed into systemic circulation. Tablet formulations are generally the first choice for drug administration because of the relative ease of both production and usage. However, for acute disorders the time of onset of action for a conventional oral tablet is generally not acceptable; this is generally attributable to gastric emptying causing a highly variable lag time between drug administration and onset of intestinal absorption.

Sublingual administration can offer an attractive alternative route of administration. The route is useful when rapid onset of action is desired. In terms of permeability, the sublingual area of oral cavity is more permeable (90µ) than cheek and

palatal areas (500-800µ) of mouth. The drug absorbed via sublingual blood vessels bypasses the hepatic first pass metabolism processes giving acceptable bioavailability with low doses and hence decreases the side effects. Sublingual drug delivery system is convenient for pediatric, geriatric and patients with dysphagia (difficulty in swallowing). The other advantages associated are their use in absence of potable water, accuracy of dosage, ease of portability, alternative to liquid dosage forms and rapid onset of action.[2]

This review is an attempt to compile various research studies undertaken in the areas of sublingual delivery of antihypertensive drugs reported in various pharmaceutical journals. Studies on buccal dosage forms and fast dissolving oral dosage forms have not been included in this review as our objective was to concentrate on sublingual delivery only.

Work Done on Sublingual Delivery of Antihypertensive Drugs:

Captopril: Captopril, an orally effective inhibitor of angiotensin converting enzyme (ACE) lowers systemic blood pressure in single dose only slightly, and effect is more marked on repeated administration. By contrast, a single dose of captopril causes substantial lowering of blood pressure in salt depleted subjects. It is rapidly absorbed from gut with a bioavailability of about 65%. The absorption is reduced by food and so it should be given 1 hour before meal.[3]

Noushin B *et al.*, formulated captopril sublingual tablet using D-optimal design. Direct compression method was used for preparing tablets and different ingredients such as polyvinylpyrrolidone (PVP), starch 1500, sodium starch glycolate etc. were used. According to this study PVP has a significant effect on tablet hardness; it was concluded that fast disintegrating captopril sublingual tablets could be achieved by using higher amount of sodium starch glycolate as well as starch 1500.[4]

Ceyhan B *et al.*, [5] compared the antihypertensive effects of sublingual nifedipine and sublingual captopril in 52 patients with hypertensive emergencies: 25 mg captopril and 10 mg nifedipine were given sublingually to 28 and 24 patients respectively. Blood pressures and heart rates were continuously measured up to 240 min post dose. A significant ($p<0.001$) hypotensive effect of both formulations occurred at 5 min and persisted for 240 min. Heart rates increased with nifedipine, but decreased with captopril. No side effect was observed in the captopril group, but tachycardia, flushing and headache were observed in 6 patients in the nifedipine group. They concluded that sublingual captopril is effective in hypertensive emergencies while captopril may prove to be an excellent alternative to sublingual nifedipine in the urgent treatment of hypertensive crisis.

Lisinopril: Lisinopril is the lysine derivative of enalaprilat and does not require hydrolysis to become active ACE inhibitor. Its oral absorption is slow (making first dose hypotension less likely) and incomplete, but unaffected by food. It undergoes extensive presystemic metabolism resulting in bioavailability of 6-60%. The duration of action is considerably longer, permitting single daily dose and ensuring uniform hypotensive action round the clock.[6]

Singh and Sameer: [7] made an attempt to provide safe pharmacokinetics requirement of plasma concentration by formulating sublingual tablet of lisinopril. Tablets were formulated using mannitol, microcrystalline cellulose and Kyron T-314 as superdisintegrants. The superdisintegrant concentration 5% w/w (Kyron T-314) was found to be optimum in all formulations. AUC of optimized sublingual tablet and marketed oral tablet was found to be 925.35µgxh/ml and 641.97 µgxh/ml with C_{max} of 60.80 µg/ml and 41.21µg/ml and T_{max} of 4h and 4h respectively. Bioavailability of optimized sublingual tablet was improved by 1.44 times as compared to oral conventional oral marketed tablet of lisinopril.

Narasimhulu *et al.*, [8] developed 10 mg lisinopril sublingual tablet and evaluated for all the physical parameters and *in vitro* drug dissolution studies. In the innovator preparation, sodium bicarbonate and sodium carbonate were used and the restriction was laid to the use of both the buffers. So, single buffer sodium carbonate was used for preparing the generic version. Special emphasis was laid on the pH of the tablet as restriction was laid in using both the buffer systems. Faster disintegration time was

achieved with optimized formula that competes with innovator formulation.

Perindopril: Perindopril is a long acting ACE inhibitor with a slow onset of action. Though 66-95% of orally administered perindopril is absorbed, only 20% is converted to the active metabolite perindoprilal. Extensive metabolism to other inactive metabolites occurs. [6]

Bhanja SB *et al.,* [9] formulated and evaluated sublingual tablets of perindopril. In this study four different groups of formulations with variation in tablet excipients were prepared by direct compression method. Weight variation, hardness, friability, drug content, disintegration time and dissolution rate for each formulation was found satisfactory.

Ramipril: Ramipril, a long-acting ACE inhibitor is almost completely metabolized to ramiprilat, which has about 6 times the ACE inhibitor activity of ramipril. Ramipril works by relaxing blood vessels, causing them to widen. Lowering high blood pressure helps prevent strokes and heart attacks. The usual dose of ramipril is 2.5-20 mg a day in two divided doses. Peak plasma concentrations of ramipril are reached within one hour following oral administration. The extent of absorption is at least 50-60% and is not significantly influenced by the presence of food in the gastrointestinal tract, although the rate of absorption is reduced. The absolute bioavailability of ramipril is 28% while its elimination half-life is about 2-4 hours.[10]

Yadav *et al.,* [11] prepared sublingual tablets of ramipril using different superdisintegrants like microcrystalline cellulose (MCC), sodium starch glycolate (SSG) and croscarmellose sodium (CCS) by direct compression method. Tablets were evaluated for pre compression and post compression parameters and were found to be in acceptable range. Sublingual table prepared with SSG and MCC was found to be the best formulation.

Vyas *et al.,* [12] formulated sublingual tablets of ramipril using different diluents like lactose, mannitol DC, dextrose anhydrous and MCC with different disintegrating agents, CCS, crospovidone and sodium starch glycolate. They observed that an optimized formulation containing 5.0 mg of ramipril, 30 mg of MCC, 59 mg of mannitol (DC) and 3 mg of SSG, 1.8 mg talc, 1mg magnesium stearate and flavor orange 0.2 ml provides a short disintegration time of 20 sec with sufficient crushing strength and acceptable friability. The optimized formulation showed better release as compared to conventional marketed tablet.

Losartan: Losartan acts as a selective angiotensin II receptor type I agonist and decreases peripheral vascular resistance. Given orally it is well absorbed and undergoes first pass metabolism in liver. It has been used to treat essential hypertension.[3]

Aghera *et al.,* [13] prepared sublingual tablets of losartan potassium by direct compression using different concentrations of starch 1500 and microcrystalline cellulose (MCC). Disintegration time of optimized formulation containing 10 mg starch 1500 and 15 mg MCC was up to 48 sec and *in vitro* release was up to 15 min. The % relative bioavailability of losartan potassium was found to be 144.7 %.

Telmisartan: Telmisartan is an angiotensin II receptor antagonist. Its concentration reaches peak plasma level within 1 hour of oral administration and has a half life of 24 hours.[14] The bioavailability of this drug is dose dependent, 42% after 40 mg oral dose and 85% following 160 mg orally.[15]

Singh B, Gupta S and Kumar A: [16] formulated sublingual tablets of telmisartan by encapsulating it in the cavity of β-cyclodextrin with the aim to improve the solubility and bioavailability of telmisartan. Direct compression method was employed using polymers like crospovidone (CP), SSG and croscarmellose sodium (CCS). Results of thickness, uniformity of weight, hardness and friability tests of prepared tablets were found to be within IP limits. Out of 6 formulations, the tablets containing 5% of CP had shown low wetting time (30.26 sec), low *in vitro* disintegration time (26.08 sec), high water absorption ratio (95.66%) and highest drug release profile (80.33%). This formulation released the drug within 3 min. The different kinetic models revealed that drug release followed non-fickian diffusion mechanism.

Reddy SG and Srinivas N:[17] developed sublingual tablets of telmisartan with the objective to obtain immediate response, escape from first pass

metabolism, reduced manufacturing difficulties and cost effectiveness. The sublingual tablet containing 1mg of telmisartan, 30 mg of MCC PH 200, 65.6 mg of mannitol (DC) and sodium starch glycolate 3 mg was found to be the best among all other nine batches of tablets since it exhibited a good dissolution profile, disintegration time, appearance, uniformity of drug content, taste and further good stability and in vivo absorption profile.

Valsartan: Valsartan is an angiotensin receptor (AT_1) antagonist. Its oral bioavailability averages 23% and food interferes with its absorption. Its elimination occurs mainly by the liver in unchanged form and has plasma half life of 6 to 9 hours.[6]

Parmar TB *et al.*, [18] formulated sublingual tablet of valsartan to overcome the first pass metabolism and provide rapid onset of action. The solid dispersion of Valsartan were prepared with different carriers like β-cyclodextrin, poloxamer 407, PEG 6000, PEG 4000, poloxamer 188 and PVP K-30. The proportion of drug and carrier were used in the ratio of 1:1 due to dose limitation of drug and solubility study was performed to select the carrier; for β-cyclodextrin molar ratio 1:1 was selected. The prepared solid dispersion was used for the preparation of sublingual tablet by direct compression. Different superdisintegrants like croscarmellose sodium, crospovidone and sodium starch glycolate were tried and optimized. Tablets were subjected to weight variation, thickness, friability, content uniformity, hardness, disintegration time, wetting time, *in vitro* drug release and *ex vivo* permeation study. Stability study as per ICH guidelines was performed for optimized formulation. Greater drug dissolution and satisfactory *in vitro* disintegration time (19 sec) was observed in optimized formulation containing drug-β cyclodextrin complex (1:1) and croscarmellose sodium (5%). Optimized formulation was found to be stable at accelerated environment condition.

Yuksel *et al.*, [19] tried to assess the effect of sublingual valsartan in a group of patients with hypertensive urgency. 80 mg of valsartan was administered sublingually to patients. At 15 min intervals blood pressure and heart rate were recorded over a 90 min period. The results of the study indicate that sublingual valsartan is an effective drug in patients with hypertensive urgency.

Amlodipine: Amlodipine has complete but slow oral absorption. The early vasodilator side effects (palpitation, flushing, headache, postural hypotension) are largely avoided. Because of less extensive and less variable first pass metabolism, its oral bioavailability is higher and more constant. Volume of distribution and plasma half life are exceptionally long. [6]

Chaudhari *et al.*, [20] used different disintegrants to prepare fast disintegrating sublingual tablets of amlodipine besylate for the potential emergency treatment of angina and hypertension. Tulsion 671 and crospovidone were used as superdisintegrants for preparing the tablets by direct compression method. All prepared tablets showed the disintegration time of less than 1 minute which was within pharmacopoeial limit. All the formulations were tested for hardness, friability, thickness and weight variation. The tablets had acceptable hardness 3.15 – 3.59 kg/cm^2 which further resulted into acceptable disintegration time 11-59 sec. Prepared formulations were also complying with the pharmacopoeial standards for weight variation. Optimized formulation of Tulsion 671 and crospovidone in combination showed disintegration time of 11 seconds and 95.89 % of drug release.

Bhardwaj V *et al.*, [21] prepared fast disintegrating tablets of amlodipine besylate by using different disintegrants and evaluated the effect of increasing amlodipine besylate load on the characteristics of fast disintegrating sublingual tablets for the potential emergency treatment of angina and hypertension. Kollidon CL, Ac-Di-Sol and sodium starch glycolate in varying concentrations (2%, 4% and 6%) were used as superdisintegrants in this study. The tablets were subjected to weight variation, hardness, friability, wetting time, water absorption ratio, disintegration time and dissolution studies. Using the same excipients, the tablets were prepared by direct compression and were evaluated in the similar way. From the results obtained, they concluded that the tablet formulation prepared with Ac-Di-Sol showed average disintegration time of 16 seconds *in vitro* that was faster than the other superdisintegrants used in the study. Also the

hardness, friability, dissolution rate and assay of prepared tablets were found to be acceptable according to standard limits. The stability studies were performed as per ICH guidelines. The optimized formulation showed no significant variations for the tablets parameters and it was stable for the specified time period.

Chinchore MV *et al.,* [22] prepared amlodipine sublingual films by using solvent casting method. The concentrations of polyvinyl alcohol (PVA), glycerin, sodium lauryl sulphate (SLS) were kept constant in all formulations and varying concentration of hydroxypropyl methylcellulose (HPMC) was used. Optimized formulation showed weight variation 90.10±0.16 mg, surface pH 6.75±0.60, folding endurance > 100, drug content 98.60±0.60%, disintegration time 17±0.30 sec and *in vitro* dissolution 98.78% at the end of 5 min

Nifedipine: Nifedipine is a calcium channel blocker available as capsules containing 5 mg and 10 mg of powder and can be used orally or sublingually. It has a bioavailability of 40–70% and plasma half life of 2 to 5 hours.[3]

Sheeba FR: [23] evaluated the effect of increasing nifedipine load on the characteristics of fast-disintegrating sublingual tablets for the potential emergency treatment of hypertension and anginal pain. Nifedipine undergoes first pass metabolism in liver and gut wall and has oral bioavailability of 43-77%. Sublingual dosage form bypasses the first pass metabolism of nifedipine and offers a fast relief from anginal pain and hypertension. An attempt was made to prepare fast dissolving tablets of nifedipine using superdistintegrants like croscarmellose sodium, sodium starch glycolate and crospovidone. Three different groups of formulations (A, R and V) with variation in tablet excipients were prepared by direct compression method. Weight variation, hardness, friability, drug content, disintegration time and dissolution time were evaluated for each formulation and found satisfactory. The studied sublingual tablet group V shows a lesser plasma half life compared to commercial oral tablet. The group V also indicates the fast dissolution and disintegration rate of the optimized nifedipine sublingual tablet, which is prerequisite for rapid management of anginal and hypertension diseases.

Prathusha P *et al.,* [24] developed nifedipine sublingual tablet by direct compression method using different concentrations of excipients. Solid dispersion were prepared with different grades of mesoporous silica by solvent loading method to improve the solubility of nifedipine. Optimized formulation showed 88 folds increase in solubility and dissolution compared with pure drug and 10 folds increase in solubility compared with marketed nifedipine tablet. Drug release followed Highuchi model.

Felodipine: Felodipoine differs from nifedipine in having greater vascular selectivity, larger tissue distribution and longer plasma half life. Due to first pass metabolism, it has bioavailability of 15-25%.[6]

Patel RJ *et al.,* [25] formulated sublingual tablet of felodipine to overcome the first pass metabolism and provide fast onset of action. The solid dispersion of felodipine were prepared with β cyclodextrin, PEG 6000, PVP K-30 and poloxamer 407 in various ratios (1:2, 1:4, 1:6, 1:8) and phase solubility study was performed to select the carrier. Sublingual tablets were prepared from the selected solid dispersion by direct compression with different superdisintegrants like croscarmellose sodium, crospovidone, kyron T-314 and sodium starch glycolate. Prepared tablets were evaluated for weight variation, thickness, friability, content uniformity, hardness, disintegration time, wetting time and *in-vitro* drug release. Stability study of optimized formulation was performed as per ICH guidelines. The optimized formulation containing drug-poloxamer 407 (1:6) complex and kyron-T314 (5%) showed greater drug dissolution (87% in 15 min) and satisfactory *in vitro* disintegration time (22 sec). Optimized formulation was found to be stable at accelerated environment condition. It was concluded that sublingual tablet of felodipine could be an alternative route to bypass hepatic first pass metabolism and avoid gastrointestinal side effects. The formulated sublingual tablets may act as a potential alternate for the felodipine oral tablet.

Nimodipine: Nimodipine is related to nifedipine but is claimed to have a preferential action on the cerebral arteries. Its use is confined to prevention of vascular spasm following subarachnoid haemorrhage. [3]

Sramika NR *et al.*, [26] prepared sublingual tablets of nimodipine to improve its bioavailability, to avoid pre-systemic metabolism in the gastrointestinal tract and hepatic first pass elimination. Different concentrations of starch 1500 and microcrystalline cellulose were used to prepare sublingual tablets by direct compression procedure. Drug polymer compatibility study was performed by FTIR spectroscopy. Preformulation property of API was evaluated. Postcompressional parameters such as disintegration time, wetting time, in vitro drug release and water absorption ratio were in acceptable range of pharmacopoeial specification. Optimized formulation was subjected to stability studies. FTIR spectroscopy study revealed that there was no possible interaction between drug and polymers. The disintegration time of optimized formulation was up to 46 sec. The in vitro release of nimodipine was up to 15 min.

Nisoldipine: Nisoldipine is a calcium channel blocker used for the treatment of hypertension, angina pectoris and congestive heart failure. It belongs to BCS Class II category and has low solubility. Due to extensive hepatic metabolism, the drug has bioavailability of only 3.7 to 8.4%.

Chatap *et al.*, [27] formulated sublingual tablets of nisoldipine with aim to improve solubility and bioavailability. NSD sublingual tablets were prepared by direct compression method utilizing two biodegradable polymers as major components; pullulan as solubility enhancer and chitosan to reduce flushing action of saliva. Tablets were further evaluated for pre & post-compression parameters and *in-vitro* drug release study. Tablets were characterized by differential scanning calorimetry (DSC), powder X-ray diffraction (PXRD) & Fourier transform infrared spectroscopy (FTIR). Formulation containing 3 % w/w pullulan and 4% w/w chitosan showed satisfactory results with disintegration time of 34 sec, wetting time of 20 sec and dissolution (98.45%) in 45 min. No interaction between drug and polymer or with other additives was observed in the DSC, XRD & FTIR studies. From this study, it can be concluded that drugs having low solubility and low bioavailability due to pre-systemic metabolism can be improved by cost effective, easy to scale up sublingual oro-mucosal approach.

Atenolol: Atenolol is a cardio selective Beta 1 blocker with insignificant intrinsic sympathomimitic activity. It reduces resting and exercise induced heart rate and myocardial contractility. It is incompletely absorbed after oral administration and is excreted largely in urine as unchanged drug.[3]

Srilatha *et al.*, [28] designed and characterized atenolol fast release sublingual tablets of atenolol prepared by using superdisintegrants like croscarmellose sodium, crospovidone and sodium starch glycolate by direct compression method. All formulations were subjected to weight variation, hardness, friability, drug content uniformity and in-vitro drug release studies as per USP monograph. The drug release rates from tablets were compared with pure drug of atenolol and it was observed that in all formulations drug released up to 99% within 30 mints only. The optimized formulation having drug, polymer and super disintegration ratio of 5:1:1 showed drug release up to 99% within 15 mints.

Bisoprolol: Bisoprolol fumarate is highly selective beta1 adrenoreceptor antagonist, which is used for the management of hypertension and prophylactic treatment of angina pectoris and heart failure. It has long duration of action. Absolute availability after a 10 mg oral dose of bisonoprolol fumarate is about 80%. Peak plasma concentrations occur within 2 to 4 hours of dosing with 5-20 mg and mean plasma value from 5 mg to 70ng/ml at 20 mg. BSP has biological half life of 10 to 12 hours.

Kharshoum RM and Ali AA: [29] prepared a novel fast disintegrating bisoprolol hemifumarate (BH) tablet formulation for sublingual administration using 2- hydroxypropyl-βcyclodextrin (HP-βCD) which forms an inclusion complex with BH to improve the permeability of the drug to sublingual membrane, and to mask the taste of the drug through the inclusion complex. Different mucoadhesive polymers such as chitosan and polyethylene glycol 6000 at different concentrations (3% and 6%) were used for reducing the flushing action of saliva and to provide enough contact time for drug to be absorbed. Eight formulation batches were prepared with variable tablet excipients.

The tablets were evaluated for the hardness, weight variation, friability, wetting time, disintegration time and dissolution studies. Optimized formulation containing high concentration of chitosan was subjected to a pharmacokinetic study using human volunteers. The bioavailability was found to be significantly higher than that of the reference (Concor®) ($p > 0.05$).

Metoprolol: Metoprolol succinate is a potent cardio selective beta-1 adrenoreceptor blocker generally used in the treatment of angina pectoris and hypertension.

Kapadia *et al.*, [30] prepared sublingual films of metoprolol succinate by different concentrations of methanol: water ratios (30:20, 25:25, 20:30). Different formulations were prepared by varying concentration of HPMC K4M and methanol: water ratio by solvent casting method. The prepared formulations were evaluated for various parameters like thickness, tensile strength, folding endurance, weight variation, % elongation, % drug content, disintegration time and *in vitro* dissolution study. Optimized batch containing hydroxypropyl methylcellulose (3.00%) and methanol: water (30:20) showed *in vitro* drug release within 4 minutes.

Timolol Maleate: Timolol maleate is a beta adrenoreceptor blocker commonly used in hypertension, angina pectoris and migraine. It is absorbed rapidly from gastrointestinal tract. Peak plasma concentration of 5 - 10 ng/ml occurs after 1 h and has a half life of 2 - 2.5 hr. About 80% of drug is metabolized in liver [31].

Gaikwad *et al.*,[32] formulated fast disintegrating sublingual tablet of timolol maleate (TM) for the potential emergency treatment of hypertension and also due to its potential to improve its bioavailability by circumventing the first-pass metabolism. Direct compression method was used to prepare tablets by incorporation of two disintegrants Ac-di-sol and sodium starch glycolate (SSG). Superdisintegrants were incorporated to break the tablet in less time period which imparts release of drug. To study the effect of independent variables (Ac-di-sol and SSG) on disintegration time and *in vitro* drug release a 3^2 factorial design was utilized. It was concluded that combination of super - disintegrants (Ac-di-sol: SSG in 3:4) showed significant ($p < 0.001$) disintegrating time, water absorption ratio and wetting time than the rest of the formulations.

Prazosin: Prazosin produces antihypertensive action by blocking alpha1 receptors in arterioles and venuoles. It is well absorbed but undergoes first pass metabolism with half life of 3-4 hours. When given orally, it produces fall in blood pressure in 4 to 5 hours and effect lasts for 12 hours. It is more effective when used along with beta blockers and diuretics.[33]

Patel *et al.*, [34] prepared sublingual tablet of prazosin by direct compression method using different agents like starch, sodium starch glycolate, microcrystalline cellulose (MCC), SSG & croscarmellose sodium (CCS). The prepared formulation batches were evaluated for weight variation, hardness, friability, drug content, wetting time, disintegration time, *in vitro* dispersion time and *in vitro* dissolution profile. All these parameters were found satisfactory.

CONCLUSION: The brief overview of different antihypertensives revealed that by delivering through the sublingual route, bioavailability and patient compliance improves by many folds. Sublingual drug delivery overcomes the difficulty in swallowing conventional tablets and capsules, among pediatric, elderly and psychiatric patients with dysphagia. A relatively rapid onset of action can be achieved which makes it important in emergency conditions. Shortcomings associated with most of the antihypertensive drugs such as low bioavailability due to first pass metabolism and drug degradation due to pH and digestive enzymes of GIT makes them an ideal candidate for sublingual administration. However all drugs cannot be given by sublingual route because the drug should have specific physicochemical properties which should be suitable to penetrate through sublingual mucosa. Although a lot of research has been done on development of sublingual dosage forms, it is surprising to see that nanotechnology has not been explored much for this route. Further work is needed to make possible more and more antihypertensive dosage forms available for sublingual use.

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