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Oral Disintegrating Film For The Treatment Of Angina Pectoris: Review

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Abstract: Pharmaceutical scientists throughout the world are trying to explore thin films as a novel drug delivery tool. Thin films have been identified as an alternative approach to conventional 38 dosage forms. The thin films are considered to be convenient to swallow, self-administrable, 39 and fast dissolving dosage form; all of which makes it as a versatile platform for drug 40 delivery. 41 Over the past few decades, tendency toward innovative drug delivery systems has majorly increased attempts to ensure efficacy, safety and patient acceptability. As discovery and development of new chemical agents is a complex, expensive and time consuming process, so recent trends are shifting toward designing and developing innovative drug delivery systems for existing drugs. Out of those, drug delivery system being very eminent among pediatrics and geriatrics is orally disintegrating films (ODFs).

Keywords: Mouth dissolving film**,** Oral cavity, Semisolid Casting Method, Rolling Method, Hot Melt Extrusion.

INTRODUCTION

The manner in which a medication is administered can have a giant have an effect on on its efficacy. Some tablets have an best attention vary inside which they supply the most benefit, however quantities outdoor of this vary may additionally be poisonous or furnish no therapeutic benefit. Limited development in the efficacy of extreme sickness treatment, on the different hand, has highlighted the want for a multidisciplinary strategy to therapeutic shipping to tissue targets.[1] As a result, new techniques to pharmacokinetics, pharmacodynamics, non-specific toxicity, immunogenicity, bio-recognition, and medicinal drug efficacy arose. Drug transport structures (DDS) are new multidisciplinary methodologies that mix polymer science, pharmaceutics, bioconjugate chemistry, and molecular biology.[2] Various drug transport and drug focused on structures are now being developed in order to forestall drug degradation and loss, take away extreme negative effects, and expand drug bioavailability and the proportion of drug amassed in the required zone. Controlled and special drug delivery, beforehand basically a pipe dream or a

possibility, is now a reality.[3] During the preceding decade and a half, pharmaceutical and different scientists carried out considerable and intensive lookup in this subject of medicine research. Examples of drug carriers encompass soluble polymers, insoluble or biodegradable microparticles, herbal and artificial polymers, microcapsules, cells, telephone ghosts, lipoproteins, liposomes, and micelles.[4] The carriers can be designed to decay slowly, reply to stimuli (such as pH or temperature), and even be centered to particular humans (e.g., by using conjugating them with precise antibodies towards positive attribute elements of the vicinity of interest). Targeting refers to the potential to direct a drug-loaded gadget to a particular region. There are two integral methods for addressing the favored areas for drug release. [5]

Introduction of Immediate Release Dosage Form

In this review and exploration, novel medication conveyance techniques are being created to extend markets/signs, protract item life cycles, and produce amazing open doors. Oral organization is the favored strategy for foundational impacts because of its usability, absence of agony, assortment, and, above all, patient consistence.[6] These strong definitions are more affordable to make since they don't need sterile circumstances. As a result of patient consistence, high accuracy dose, and creation economy, tablets are the suggested strong portion structure. Excipients and hardware choices will be seriously impacted in the event that strong measurements structure advancements change in response to noteworthy enhancements in drug improvement, like genomics.[7] The advancement of further developed oral protein conveyance innovation as moment discharge tablets that can deliver prescriptions all the more rapidly is particularly encouraging for ineffectively dissolvable medications like high atomic weight protein and peptide.[8] The oral course stays the best course for directing helpful specialists because of its minimal expense of treatment, simplicity of assembling, and simplicity of organization.[9] Therefore, patient consistence is very high. Numerous patients require a quick beginning of activity in a particular restorative condition, requiring prescription delivery at the earliest opportunity. About portion of the populace is impacted, bringing about a high pace of insufficient treatment.[10]

Pharmacokinetics

This field researches assimilation, conveyance, digestion, and discharge. The rate and measure of retention are significant on the grounds that medication focus arrives at restorative levels following assimilation and subsequently advances pharmacological movement. Customary portion definitions slow crumbling, bringing about quick disintegration.[11] Tissue porousness, perfusion rate, drug restricting to tissue, disease status, drug cooperation, and different factors all impact medicine circulation.[12] The length and strength of a not entirely set in stone by the pace of medication leeway from the body or the site of activity, for example biotransformation. A lessening in liver volume and provincial blood stream to the liver eases back drug biotransformation through oxidation, decrease, and hydrolysis.[13] The half-existence of medications released by the kidneys increments as renal freedom eases back.[14]

Standard for Immediate Release Drug Delivery System[15]

1. Immediate release dosage form should
2. In the case of solid dosage, it should dissolve or disintegrate quickly in the stomach.
3. It should be compatible with taste masking in the case of liquid dose forms.
4. Be portable without worrying about fragility.
5. Have a pleasant taste in your tongue.
6. After oral administration, it should leave little or no residue in the mouth.
7. Low sensitivity to environmental factors such as humidity and temperature
8. Be produced at a minimal cost utilising traditional processing and packaging equipment
9. Rapid solubility and absorption of the drug, resulting in a quick commencement of effect.

Excipients Standards

Excipients balance the qualities of the actives in quick delivery dose structures. An exhaustive comprehension of the science of these excipients is fundamental to keep away from cooperations with the actives. One more test looked by formulators is laying out the expense of these synthetics.[16] Excipients are fundamental in the advancement of quick softening tablets. These dormant food-grade synthetics give the appropriate organoleptic highlights and item execution when included the detailing. Excipients, except for certain actives that require veiling specialists, are general and can be utilized for a wide scope of actives.[17]

Anatomy of Oral Cavity

The oral pit is underneath the nasal depressions on the face's front side. Its lines are characterized by a rooftop, a story, and parallel dividers.[18] The front of the mouth opens to the face through the oral gap, while the rear of the mouth connects to the oropharynx by the oropharyngeal isthmus (likewise named the isthmus of the fauces). The oropharyngeal isthmus is encircled by the delicate sense of taste and palatoglossal curves. The unpaired mandible, sphenoid, and hyoid bones, as well as the combined maxillae, palatine, and transient bones, all add to the mouth pit's construction.[19] The oral depression is partitioned into foremost and back districts by the dental curves (or teeth): the front oral vestibule is tracked down foremost to the teeth and behind the lips, while the oral hole legitimate is found behind the teeth. Salivary organs dampen within the mouth and help in food absorption by emitting catalysts that assist carbs with separating quicker. The organs at concern are the parotid, submandibular, and sublingual organs.[20]

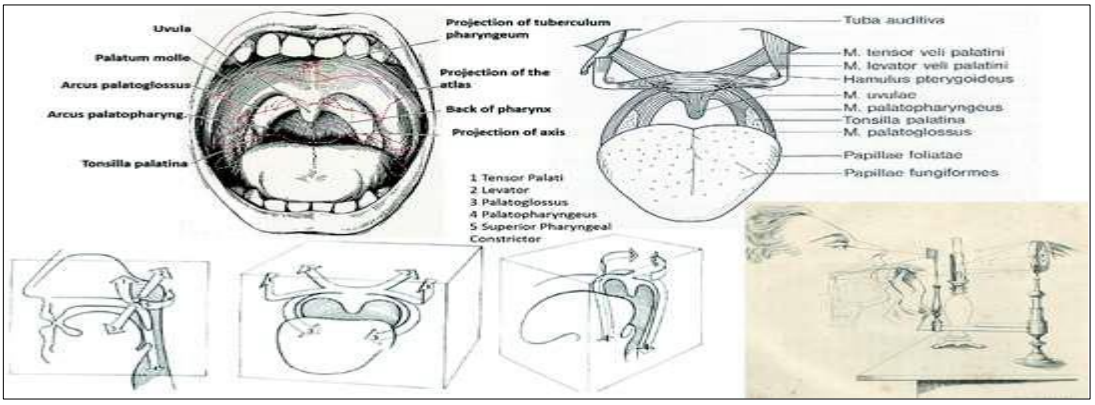

Figure no 1: oral cavity

Oral Mucosa

The wet coating of the mouth cavity is the oral bodily fluid film, frequently known as the oral mucosa. Oral mucosa has attributes of both skin and gastrointestinal mucosa, and is histologically of a momentary sort. The oral mucosa has various capacities.[21] A portion of these capacities incorporate security, reasonableness, heat control, discharge, immunological action, and ingestion.

Protection

The significant capacity of the oral mucosa as a surface coating is to isolate and safeguard the oral pit's more profound tissues and organs from the climate.[22] The oral delicate tissues are exposed to mechanical powers like pressure, extending, shearing, and surface scraped area because of seizing, gnawing, and biting food. The epithelium and connective tissue of the oral mucosa adjust to endure the conceivable pressure actuated by these exercises.[23] A solid basal turnover of epithelial cells makes up for grinding misfortunes. Since microbial specialists don't stick to the surface cells of the mucosa because of fast surface reestablishment, microbial colonization is by implication restricted. Besides, on the grounds that to the quick basal turnover, twisted recuperating in the oral depression is quicker and more compelling. Accordingly, the oral mucosa epithelium goes about as the primary defensive boundary against hurtful synthetics.[24]

Sensation

The mouth mucosa's tactile action gives data. The oral mucosa has receptors that recognize temperature, contact, agony, and taste. Sucking, choking, spewing, and salivation are totally set off by these receptors. In the cerebrum, there are additionally particular sensors that react to the flavor of water and produce thirst.[25]

Secretion

The oral mucosa's principle emission is salivation, which is delivered by the salivary organs and keeps up with the mouth mucosa wet. The three head salivary organs in people are the parotid, submandibular, and sublingual salivary organs.[26] These organs are encased and situated external the mouth, with long channels bringing their emissions through the mucosa. The labial, lingual, palatal, buccal, glossopalatine, and

retromolar organs are a gathering of little salivary organs in the mouth. These unencapsulated organs are arranged inside the mucosal films and have more limited channels.

Immune Mucosal Network

The oral cavity contains a few safe framework parts. Models incorporate gingival sulcus incendiary cells, epithelial Langerhans cells, and oral tonsillar tissues. Other invulnerable framework parts in typical oral tissues, like mucosal-related lymphoid tissue (Malt), assume a part in antigen handling and show, immune response arrangement and delivery, and cellinterceded effector pathways.[27]

Absorption

In spite of the way that the oral epithelium has no absorptive capacity, porousness shifts in view of epithelial hindrance thickness, development design, and the shortfall of the layer corneum in various oral areas. The mouth's floor, which is one of the most slender epithelial areas, might be more permeable than different pieces of the body. This could clarify why a few medications can be ingested through the mouth (salicylic corrosive, dynamite, and so on) Blood seepage from the oral depression straightforwardly into the fundamental dissemination upgrades this drug conveyance pathway.[28]

Saliva and Its Composition

The liquids discharged by the major and minor salivary organs make up salivation. The day by day volume of spit emitted by individuals is 1-1.51. Salivary stream is diurnal, with the most reduced levels happening during rest and a fairly steady benchmark level all through waking hours, with set off stream intensifications. Basal rates in grown-ups range from 0.3 to 0.5 ml/min. Salivation is comprised of 99.5 percent water and 0.5 percent solutes artificially (electrolyte parts, catalyst and other salivary proteins) (electrolyte parts, chemical and other salivary proteins). The emissions of various organs contrasted enormously. The watery, amylase-rich serous salivation discharged by the parotid organs, the gooey spit emitted by the sublingual organ, and the mucinous spit emitted by the submandibular organ.[29] Since numerous proteins in salivation are quickly eliminated by appending to the hydroxyapatite of teeth and oral mucosal surfaces, blended spit isn't simply the amount of these releases. Spit's pH goes from 5.8 to 7.4, but it gets more isotonic and basic as it is discharged all the more rapidly. Salivary stream rate is impacted by the sort of taste boosts. By and large, citrus extracts or acrid food varieties cause the most noteworthy stream rate and Na+ levels, while salt causes high protein and CaH levels. Spit contains an assortment of salts, including chlorides, bicarbonates, sodium and potassium phosphates, and calcium phosphates. broken up gases and natural atoms, for example, urea, uric corrosive, serum egg whites, globulin, mucin, the bacteriolytic compound lysosyme, and the processing chemical salivary amylase are completely found in typical spit (ptyalin). Lactoperoxidase, blood bunch antigens, EGF, VIP, RNAase, DNAase, lingual lipase, kallikrein, and lactoferrin are among different compounds distinguished. Iodine, which is additionally contained in spit, is found in salivary organs.[30]

Swallowing (Deglutition)

Food and salivation are moved from the mouth to the stomach through gulping, which is a directed strategy. A complicated reflex reaction called gulping is set off by afferent driving forces in the trigeminal, glossopharyngeal, and vagus nerves. These motivations are coordinated

by the core of the tractus solitaries and the core questionable. The efferent filaments to the pharyngeal muscular structure and the tongue are conveyed by the trigeminal, facial, and hypoglossal nerves. Gulping starts when the substance of the mouth are deliberately assembled on the tongue and constrained in reverse into the throat.[31]

Introduction of Mouth Dissolving Film

The oral course of medication organization is the most liked because of its simplicity of organization, painlessness, versatility, patient consistence, and acknowledgment. Utilizing current novel advancements, numerous options in contrast to the oral course of medication conveyance have been proposed for pediatrics, geriatrics, sick, and rebelliousness patients. Bioadhesive mucosal measurements structures like cement tablets, gels, and fixes have been created because of innovative forward leaps.[32] The utilization of polymeric movies to convey drug into the buccal pit has recently showed huge potential among the different portion structures. After deterioration as well as disintegration, orally breaking down films (ODFs) quickly hydrate by splashing salivation, letting the dynamic pharmacological part out of the measurements structure. ODFs are a kind of detailing that utilizes hydrophilic polymers to break up rapidly when presented to spit. Oral breaking down tablets (ODTs) and oral crumbling films are two sorts of orally deteriorating drug conveyance frameworks (ODFs). These frameworks were created in the last part of the 1970s as an option in contrast to standard dose structures such fast deteriorating tablets and containers for geriatric and pediatric patients who experienced issues gulping customary measurement structures. A standard ODF is about the size of a postage stamp. The appearance of ODT in the commercial center was intently attached to patient advising about right organization, with guidance like "don't bite/don't swallow." Despite these standards, biting and gulping occasions were ordinarily archived. Then again, ODFs freed the majority from these calamities.[33]

Special Features of Mouth saliva Dissolving Films

1. A finely thin film
2. Negative in nature
3. Comes in a variety of sizes and forms
4. Rapid decomposition
5. Quick release
6. Make the mouth feel good.
7. Have a good sense of taste.
8. No residues should be left in the mouth cavity.

Formulation Aspects For Mouth Saliva Dissolving Films

ODFs can contain allergy medicines, hostile to diarrheals, antidepressants, vasodilators, enemies of asthmatics, against emetic drugs, etc. ODFs' flavor can in like manner be masked with dimenhydrinate. ODFs regularly contain salbutamol sulfate, rizatriptan benzoate, verapamil ondansetron, dexamethasone, rofecoxib, cetirizine, pilocarpine, tianeptine sodium, indomethacin, and different meds.

Film Forming Polymer

Water-solvent polymers are utilized as film formers since they consider quick breaking down, a lovely mouth feel, and mechanical strength. The sort of polymer utilized and the sum used in the details decide the strip's strength. The most normally involved polymers for film creation are pullulan, gelatin, and hypromellose. Pullulan, gelatin, guar gum, thickener, HPMC, changed starches, PVPK30, PVA, and other water-solvent polymers are a couple of models.

Ideal properties of the polymers used in the oral film

1. Nontoxic, aggravation free, and boring polymers ought to be utilized.
2. It ought to be flavorless.
3. It ought to be without poisons that can be drained.
4. It should be modest and easy to get.
5. During the deterioration interaction, it ought not be a staggering impediment.
6. It should have an extensive timeframe of realistic usability and not cause optional disease.

Plastisizers

Plasticizers further develop mechanical properties like as rigidity and percent stretching in many details. Plasticizer fixations ordinarily range from 0% and 20% weighted normal. Plasticizers like PEG, glycerol, diethyl phthalate, triethyl citrate, tributyl citrate, and others are regularly utilized.

Sweetening Agent

Sugars have turned into a famous fixing in food sources and prescriptions intended to break up or deteriorate in the mouth. Normal and counterfeit sugars are utilized to build the attractiveness of oral dissolving details.

(1) A characteristic sugar that is water solvent, like xylose, ribose, glucose, sucrose, maltose, stevioside, and others.

(2) Water-solvent fake sugar: sodium or calcium saccharin salts, acesulfame-K, and so forth Aspartame is a sugar comprised of dipeptides.

Saliva Stimulating Agent

Salivary energizers, which are by and large acidic in nature, help to separate ODFs by expanding spit creation in the buccal cavity. Probably the most regularly utilized salivation animating mixtures incorporate citrus extract, malic corrosive, tartaric corrosive, ascorbic corrosive, and lactic corrosive.

Surfactant

Surfactants are utilized as solubilizers, wetting specialists, and dispersants, making the film deteriorate like a flash and the dynamic fixing to be delivered right away. Surfactants likewise help the disintegration of ineffectively solvent medications in quick dissolving buccal movies. A few models are Polaxamer 407, sodium lauryl sulfate, benzalkonium chloride, benzthonium chloride, tweens and ranges, and others.

Flavor

Flavors are fundamental for veil the harsh or horrendous taste of the coordinated medication. How much still up in the air by the strength and nature of the flavor. Any flavor endorsed by the FDA in the United States, like sweet, sharp, or mint, can be utilized. As per one review, a flavor blend of mint, licorice, and sucralose successfully covers the harsh taste of diclofenac sodium. Electronic tongues are utilized to recognize the impacts of different taste concealing specialists (TMAs).

Colouring Agent

Whenever part of the plan fixings or medications are in insoluble or suspension structure, shades, for example, titanium dioxide or FD&C supported shading added substances are utilized in oral strips (at fixations not surpassing 1% w/w).

Method of film formulation

There are almost 4 method foe the film formulation

1. Solvent casting method
2. Hot Melt Extrusion
3. Semisolid Casting Method
4. Rolling Method

1. **Solvent casting method** [33]

The most average methodology for assembling ODFs with water dissolvable excipients, polymers, and drugs broke up in de-ionized water is dissolvable projecting; as a result, a homogenous combination is accomplished by utilizing high shear powers produced by a shear processor. The pre-arranged arrangement is poured onto a petri plate and the dissolvable is permitted to dry by presenting it to high temperatures to create great quality movies. The dissolvable projecting strategy was utilized to make an orodispersible film of tianeptine sodium utilizing different grades of Lycoat and HPMC. In the dissolvable projecting procedure, the film framing polymer is generally absorbed a reasonable dissolvable short-term. In view of basic physicochemical highlights of the API, like softening point, shear responsiveness, and polymorphic structure, the kind of API that should be remembered for ODF characterizes the ideal dissolvable. The medication's similarity with the dissolvable and other excipients is considered prior to finishing a detailing. The presence of caught air rises during the detailing system can affect the consistency of the completed film. With the assistance of a vacuum siphon, the blend is deaerated. The dissolvable projecting strategy was likewise utilized to make a mosapride orodispersible film definition. In the projecting system, the consistency of the answer for be poured is vital.

Figure no: 2 Solvent casting method flow chart

2. Hot Melt Extrusion

In hot-liquefy expulsion, dry parts for the film are warmed and homogenized by an extruder screw until they are liquid and blended. The extrudate is driven into the fundamental film shape by a level expulsion kick the bucket. Lengthening rollers can influence the thickness and strength of the film while it is as yet hot and adaptable. In the wake of cooling and cutting the expelled film, the hot soften expulsion procedure is talked about.

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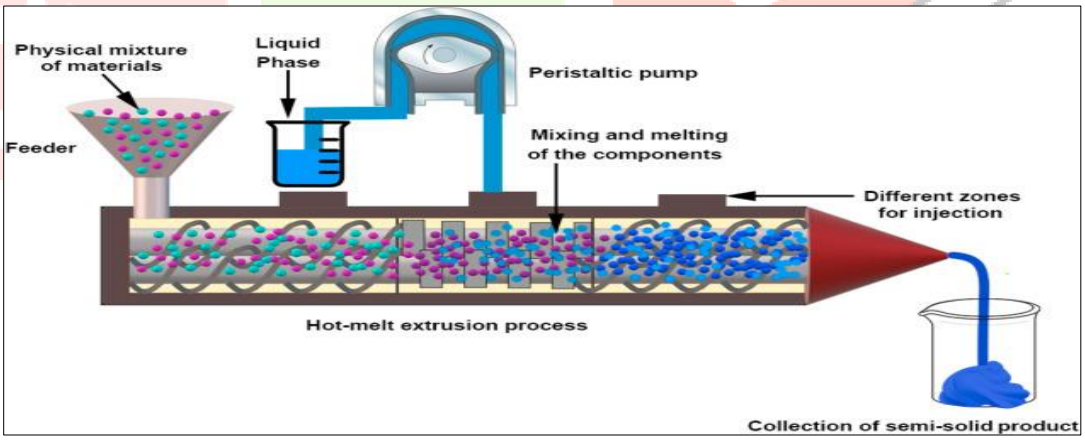

Figure no: 3. Hot Melt Extrusion

3. Semisolid Casting Method

A film-shaping polymer arrangement that is water solvent is made. The resultant arrangement is joined with a polymer arrangement that is corrosive insoluble (for example cellulose acetic acid derivation phthalate, cellulose acetic acid derivation butyrate). To acquire gel mass, an adequate measure of plasticizer is utilized. At last, the gel mass is shaped into the movies or strips utilizing heat-controlled drums. Somewhere in the range of 0.015 and 0.05 creeps of film thickness ought to be utilized.

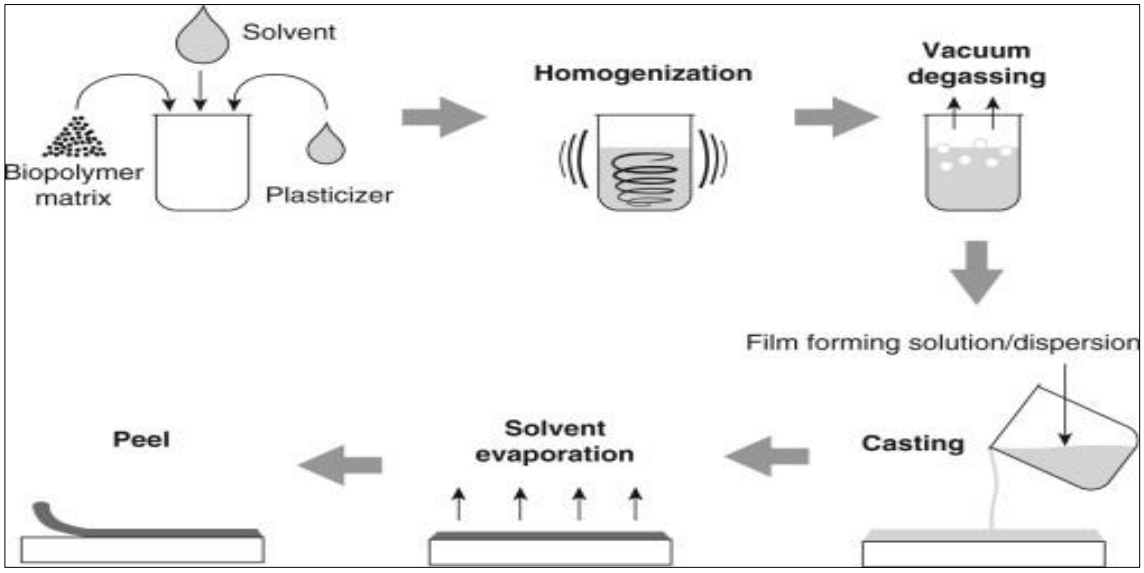

Figure no. 4: Semisolid Casting Method

4. Rolling Method

This strategy includes making a pre-blend, adding a functioning, and afterward producing a film. Set up a pre-blend in with a film-framing polymer, a polar dissolvable, and different added substances (barring a medication) and add it to the expert clump feed tank. A first metering siphon and control valve ought to be utilized to take care of it to either of the first and second blenders. Add the required measure of medicine to the blender you've chosen. Consolidate the drug with the expert cluster pre-blend to get a uniform grid. Second metering siphons convey a foreordained measure of uniform framework to the dish. At long last, the film is framed and shipped to the help roller on the substrate. The wet film is dried by means of controlled base drying. The most generally utilized solvents are water and a combination of water and liquor.

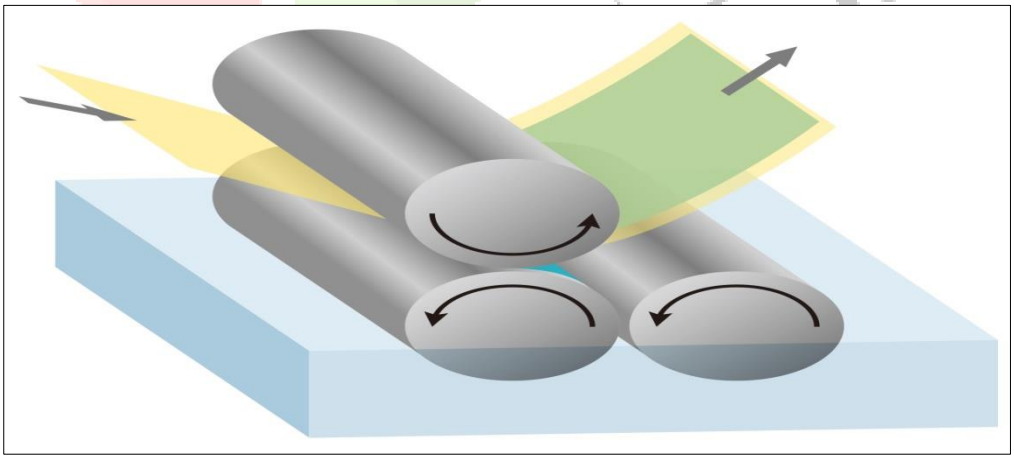

Figure no. 5: Rolling Method

Evaluation Parameters

1. Thickness Test
2. Tack Test
3. Youngs Modulus
4. Tail flick Test
5. Thermodynamic Stability Study
6. Drug Content
7. Viscosity
8. Tensile Strength
9. Folding Endurance
10. Weight of films
11. % Elongation
12. Swelling Properties
13. Disintegration Time
14. Surface pH
15. Content Uniformity
16. Dissolution test

Table no. 1: Marketed Preparation of Mouth Dissolving Film

Product	API	Manufacturer	Use
Listerine	Cool Mint	Prfizer	Mouth Ulcer
Benadryl	Diphenylhydramine HCL	Prfizer	Antiallergic
Suppress	Menthol	InnoZen,® Inc	Cough Suppressant
Klonopin wafers	Clonazepam	Solvay Pharmaceutical	Antianxiety
Theraflu	Dextromethorphan	Novartis	Antiallergic
Orajel	Menthol/Pectin	Del	Mouth Freshner

ANGINA PECTORIS

Angina pectoris is chest pain or discomfort that occurs when a part of your heart doesn't get enough blood and oxygen. It is most often just called angina. Angina can be a symptom of coronary artery disease (CAD). But it can have other causes.

Figure no. 6: Burning of Heart

ANGINA PECTORIS.

Angina pain is often described as squeezing, pressure, heaviness, tightness or pain in the chest. It may feel like a heavy weight lying on the chest. Angina may be a new pain that needs to be checked by a health care provider, or recurring pain that goes away with treatment. Although angina is relatively common, it can still be hard to distinguish from other types of chest pain, such as the discomfort of indigestion. If you have unexplained chest pain, seek medical help right away.

Types

There are different types of angina. The type depends on the cause and whether rest or medication relieve symptoms.

Stable angina. Stable angina is the most common form of angina. It usually happens during activity (exertion) and goes away with rest or angina medication. For example, pain that comes on when you're walking uphill or in the cold weather may be angina. Stable angina pain is predictable and usually similar to previous episodes of chest pain. The chest pain typically lasts a short time, perhaps five minutes or less.

Unstable angina (a medical emergency). Unstable angina is unpredictable and occurs at rest. Or the angina pain is worsening and occurs with less physical effort. It's typically severe and lasts longer than stable angina, maybe 20 minutes or longer. The pain doesn't go away with rest or the usual angina medications. If the blood flow doesn't improve, the heart is starved of oxygen and a heart attack occurs. Unstable angina is dangerous and requires emergency treatment.

Variant angina (Prinzmetal angina). Variant angina, also called Prinzmetal angina, isn't due to coronary artery disease. It's caused by a spasm in the heart's arteries that temporarily reduces blood flow. Severe

chest pain is the main symptom of variant angina. It most often occurs in cycles, typically at rest and overnight. The pain may be relieved by angina medication.

Refractory angina. Angina episodes are frequent despite a combination of medications and lifestyle changes.

SYMPTOMS

Angina symptoms include chest pain and discomfort. The chest pain or discomfort may feel like:

1. Burning
2. Fullness
3. Pressure
4. Squeezing

Pain may also be felt in the arms, neck, jaw, shoulder or back

Other symptoms of angina include:

1. Dizziness
2. Fatigue
3. Nausea
4. Shortness of breath
5. Sweating

The severity, duration and type of angina can vary. New or different symptoms may signal a more dangerous form of angina (unstable angina) or a heart attack. Any new or worsening angina symptoms need to be evaluated immediately by ahealth care provider who can determine whether you have stable or unstable angina.

Angina in women

Symptoms of angina in women can be different from the classic angina symptoms. These differences may lead to delays in seeking treatment. For example, chest pain is a common symptom in women with angina, but it may not be the only symptom or the most prevalent symptom for women. Women may also have symptoms such as:

1. Discomfort in the neck, jaw, teeth or back
2. Nausea
3. Shortness of breath
4. Stabbing pain instead of chest pressure
5. Stomach (abdominal) pain

Description about Angina Pectoris [34]

Cardiovascular disease is the most frequent cause of death in the United Kingdom. Coronary heart disease (CHD) accounts for 65 % of cardiovascular deaths in men and for about half of deaths in women (OPCS, 1989). In both sexes up to the age of 65 years, cardiovascular diseases account for up to a quarter of all years of working life lost (OPCS, 1987). Coronary heart disease commonly presents as angina pectoris. Angina affects over one million men and women under 65 years age in the United Kingdom (Shaper, 1984; Smith, 1990). It is the initial clinical manifestation of CHD in over a third of men and in about two-thirds of women (Kannel, 1972). The first description of angina pectoris as a clinical syndrome over 200 years ago (Heberden, 1772) was followed by the anatomical association with coronary atheroma and establishment of the ischaemic theory of angina (Proudfit, 1983). It is now recognised that although there is a close relationship between angina, myocardial ischaemia and coronary atherosclerosis, any one of these three can exist on its own, or in combination with one or both of the other two entities. The majority of patients with angina pectoris present to their general practitioner and are managed in the community but little is known about the frequency, prognosis and optimum investigation and management of this manifestation of coronary disease in the population. Prevalence of angina has been estimated in many cross-sectional surveys using questionnaires, but incidence is less well documented and there has been no contemporary incidence study since the advent of revascularisation. Clinical characteristics of patients presenting with angina pectoris in the general population beyond a resting ECG have not been defined. Electrocardiography - resting, exercise and ambulatory - features foremost among the investigations for patients presenting with angina pectoris. Continuous ambulatory electrocardiographic monitoring was introduced nearly two decades ago, yet despite extensive investigation, its frequency and prognostic value in patients presenting with angina pectoris in the general population have not been documented. This chapter reviews the prevalence and incidence of angina pectoris and the frequency and prognostic significance of resting, exercise and in particular, ambulatory electrocardiography in patients with angina. Careful attention is paid to the method of patient selection in the reported studies to assess whether their results can be applied to the generality of stable angina patients encountered in clinical practice. The limitations of available data are discussed, and the objectives of the present study are outlined.

Prevalence of Angina

Prevalence of angina has been estimated in three large studies (Table 2) using a chest pain questionnaire and ranges from 4.8% in middle-aged men to 8.5% in women. Epidemiological methods have to be simple and cheap so most surveys are limited to captive populations in particular employments (Reid et al, 1974) and to pecific age groups.

Table no.2: Patient Data

Sr.No	Patients	Civil Service	Indian Regional Heart Study	British Regional Heart Study
1	Sex	Men	Men	Men & Woman
2	Age Year	40-60	40-50	40-59
3	N=	18403	7735	10359
4	Prevalence (%)	4.8	4.8	Men 6.3 Women 8.5

Prevalence of angina pectoris

Two other community based surveys of patients under treatment for ischaemic heart disease also report angina prevalence. In a 4-month survey in 1979 by the Royal College of General Practitioners, 51 general practitioners in Newcastle covering a population of 125,000 recorded patients aged 30-59 years that they treated for angina, and concluded that prevalence in their population was 1.1% (RCGP research committee, 1982). The methods used in this survey include memory recall to identify treated cases and a diagnosis which includes a 'suggestive' history of angina. Both methods have obvious limitations. A more reliable estimate of prevalence comes from a survey of prescriptions for nitrates in Nottingham (population 612,800). During a 6-month period in 1984-5 15,451 nitrate prescriptions for 6,856 patients were identified (Cannon, 1988). Estimated prevalence of angina was 1.5% in men under 65 years age and 0.6% in women under 60 years. However this may be an overestimate of the true prevalence as the diagnosis of angina examined in a sub sample of patients was incorrect in a significant proportion. In that study, prevalence increased sharply in men over the age of 65 years to 7.1% and to 4.4% in women over 60 years old.[35]

Incidence of Angina

Incidence of angina pectoris has proved difficult to measure. To date, only the Framingham study has estimated incidence in a representative sample of men and women in the general population (Kannel, 1972). A cohort of 5,127 residents of Framingham, USA underwent biennial clinical examination between 1949 and 1966. From 303 cases of angina arising in men and women aged 33 to 69 years over this period, incidence estimates in men ranged between 2/1000 population/year in the 40- 44 year age group to 11/1000/year in the 55-59 year age group. Corresponding rates in women were 0.5/1000/year to

2/1000/year. The incidence of angina has also been reported in three other areas in an occupational cohort of 9,764 Israeli male civil service and municipal employees (Medalie, 1976), in a single London general practice population (Fry, 1976) and in a population of men from selected general practices in Edinburgh with easy access to a special clinic.[30]

PATIENT CHARACTERISTICS AND CHEST PAIN CLINIC

Patients referred

The open access Chest Pain Clinic was set up solely for the purposes of this study. A total of 489 patients were referred to this clinic between June 1990 and March 1992. At all ages, there were more male than female patients. Twenty-two patients did not meet the criteria for eligibility for clinic referral. Of these, 12 were aged 71 years or over, 7 patients had a past history of coronary heart disease, and 3 patients were referred from outside the registered study population. One hundred and ten consecutive patients who presented with typical angina pectoris were included in the study. Sixty-three per cent (n=70) were male, and 37% (n=40) were **female.**

The remainder of referrals were classified as follows (section 2.9): n=63 (13%) with possible angina; n=63(13%) with 'atypical pain ? cause'; n=204 (44%) with non-cardiac pain, and 27 (6%) patients were admitted to the coronary care unit because the history and/or electrocardiogram was consistent with unstable angina or myocardial infarction.

Symptom Characteristics

The duration of angina symptoms reported prior to initial assessment at the Chest Pain Clinic was observe Although the majority of patients were assessed within 24 hours of their general practitioner first suspecting a diagnosis of coronary heart disease, 61 % of patients reported experiencing angina for longer than one month prior to the clinic visit. Ten per cent reported the presence of symptoms for more than one year.

Cardiac Risk Factors

Hypertension

Hypertension was defined as a systolic blood pressure of >160 mmHg and/or a diastolic blood pressure of > 100 mmHg on at least two recordings, or when the patient was receiving antihypertensive medication. A higher cut-off for diastolic blood pressure was used to allow for clinic readings. Prevalence of hypertension in patients with angina (Figure) was 48% (53 of 110). In the 53 patients with hypertension, raised blood pressure had been previously undetected in 26%, detected but not treated in 34%, and inadequately treated in 17%.

Hypercholesterolaemia

The distribution of random serum cholesterol measurements is Total serum cholesterol level was > 6.5 mmol/L in 75% of patients with typical angina, and > 9 mmol/L in 12% of these patients. There was no significant difference in the proportion of patients with a family history of coronary heart disease among those with a cholesterol level > 6.5 mmol/L compared with a level < 6.5 mmol/L (53% vs 38%, p = 0.15). In all but one patient, hypercholesterolaemia had been previously unrecognised.

Smoking, diabetes, and obesity

The prevalence of current cigarette smokers among patients with typical angina was 30%. A further 38% were ex-smokers, 23% lifelong non smokers and 9% pipe or cigar smokers. Ex-smokers had given up smoking for at least one year. Obesity, defined as a body mass index > 30 kg/m2, was prevalent in 27% (30 of 110) of patients with typical angina. A random plasma glucose level > 1 1 mmol/L was detected in two patients with angina who were not known diabetics. A further 7 (6%) patients had previously diagnosed diabetes mellitus. The proportion of patients presenting with typical angina in the general population who had major cardiovascular risk factors was high: 82% of patients had one risk factor, and almost a third (32%) had two major cardiovascular risk factors.

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