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## Plasticizers: A Vital Excipient in Novel Pharmaceutical Formulations

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#### ABSTRACT

Plasticizers have got significant role in pharmaceutical formulations because of their vital importance in the formulations like gastro-retentive films, ocular films, transdermal films, buccal films, oro-dispersible films. Flexibility, Endurance, Resistibility and Stability which are suitable properties of formulation could be easily achieved by using plasticizers which ultimately imparted desired characteristic in the formulation by the radical use of this excipient. In this review an effort was made to disclose importance, theories and plasticizers mechanism in different novel pharmaceutical formulations to understand its versatility efficiency, utility and tendency to modified different novel pharmaceutical formulations.

**Key words:** Modification, Formulations, Plasticizers, Films.

### 1. INTRODUCTION

Plasticizer is an important and versatile excipient of pharmaceutical formulations. It helps in improving the flexibility of the film and reduces the brittleness of the formulations. Plasticizer significantly improves the strip properties by reducing the glass transition temperature of the polymer. The selection of plasticizer depends upon many factors including its compatibility with the formulation excipients, drug and also on the type of solvent employed in the formulation of pharmaceutical formulation.<sup>1</sup>

Plasticizer can decrease glass transition temperature of polymer in the range of 40–60°C for non-aqueous solvent system and for aqueous system below 75°C. The Plasticizer employed should impart the permanent flexibility to the film formulation and it depends on the volatile nature of plasticizer and the type of interaction of plasticizer with the polymer. It should be compatible with drug as well as other excipients used for preparation of film.<sup>2</sup>

The effects of these plasticizers can be determined by determining glass transition temperature, tensile strength, percent elongation, and Young's modulus of the prepared pharmaceutical formulations.<sup>3</sup>

## 2. PROPERTIES OF PLASTICIZERS<sup>4-6</sup>

1. Plasticizer is a key ingredient for the quick dissolving films. It significantly enhances the film forming properties by diminishing the glass transition temperature of the polymer.
2. Plasticizer serves to enhance the flexibility of the strip and reduces the brittleness of the films.
3. The chemical structure and concentration of plasticizers play an important role in alleviating the glass transition temperature of the polymers.
4. The selection of plasticizer depends on its compatibility with the polymer and also the type of solvent employed in the casting of the film.
5. The flow of polymeric solution gets better with the use of plasticizer and improves the strength of the polymer. Glycerol, Propylene glycol, low molecular weight polyethylene glycols, citrate derivative such as tributyl, triethyl, acetyl citrate, triacetin and castor oil are commonly used phthalate derivatives like dimethyl, diethyl and dibutyl phthalate, citrate derivatives utilized plasticizer excipients.
6. Typically the plasticizers are used in the concentration of 0–20 percent w/v of dry polymer weight. However, inappropriate use of plasticizer may prompt to film breaking, splitting and peeling of the strip.
7. It is also reported that the use of certain plasticizers may also affect the absorption rate of the drug.

## 3. THEORY OF PLASTISIZERS

There are several theories that explain the effects of plasticizers and their combination which allows to explain the concept of polymer plasticization.<sup>6-8</sup>

### 3.1 Gel theory

Polymers are formed by an three-dimensional internal network of weak secondary bonding forces (van der Waals' forces, hydrogen bonding) sustained by loose attachments between the polymer molecules along their chains. These bounding forces are easily minimize by external strain applied to the material, allowing the plasticized polymer to be bend, stretch, or compress. Plasticizer molecules attach along the polymer chains, reducing the number of the polymer-polymer attachments and hinder the forces holding polymer chains together. It separates the polymer chains and increases the space between polymer molecules and thus reducing the rigidity of the gel structure. Moreover, plasticizer molecules that are not attached to polymer tend to aggregate and allow the

polymer molecules to move more freely, and that is the reason how plasticizer enhancing the gel flexibility.

### 3.2 Lubricity theory

It states that plasticizer acts as a lubricant, reducing intermolecular friction between polymer molecules that are responsible for rigidity of the polymer. On heating, the plasticizer molecules slip between polymer chains and weaken the polymer-polymer interactions (van der Waals' forces), shielding polymer chains from each other. This prevents the reformation of a rigid network, resulting in more flexible, softer and distensible polymer matrix.

### 3.3 Free volume theory

The glass transition temperature ( $T_g$ ) of the polymer gets reduced by the presence of plasticizers. Free volume is a measure of internal space available within a polymer matrix. There are three important sources of free volume in polymer (a) motion of polymer end groups, (b) motion of polymer side groups, and internal polymer motions. When the free volume increases, more space or free volume is available for polymer chain movement also increases. A polymer in the glassy state has an internal structure with molecules packed closely and small free volume. This makes the material rigid and hard. When the polymer is heated to above the glass transition temperature, the thermal energy and molecular vibrations create additional free volume which allows higher internal chain rotation and an increase in the mobility of segment. This ultimately makes the system more flexible and rubbery. When small molecules such as plasticizers are added, the free volume of polymer chain segments increase and decrease the glass transition temperature.

Mechanistic theory of plasticization considers that plasticizer molecules are not bound permanently to the polymer, but rather there is a dynamic exchange process whereby, a constant associations and disassociations of polymer-polymer, polymer plasticizer and plasticizer-plasticizer molecules form. Some plasticizers form stronger associations with polymer than others. At low plasticizer levels, the plasticizer polymer interactions are the dominant interactions, what explains "antiplasticization". At high plasticizer loadings plasticizer-plasticizer associations predominate.

## 4. MECHANISM AND TYPES OF PLASTICIZERS

In order to get better plasticizing effect, it should be thoroughly mixed and incorporated into the polymer matrix. This can be obtained by heating and mixing until either the resin dissolves in the plasticizer or the plasticizer dissolves in the resin.

The plasticized material is then molded, casted or shaped into the useful desirable product and cooled. Different plasticizers exhibit different characteristics in both the ease with which they form the plasticized material and in the resulting mechanical and physical properties of the flexible and stable product.<sup>10</sup>

The mechanism of plasticization is due to interpose between every individual strand of polymer and thereby causing breakdown of polymer-polymer interactions. The tertiary structure of the polymer is converted into more porous, flexible and with less cohesive structure. Plasticizers soften and swell the polymer which aids in overcoming their resistance to deformation. Plasticized polymer would deform at a lower tensile force as compared to without plasticizer. This enhances the polymer – plasticizer interaction. This effect in turn enhances the film elongation effect. The interaction to a greater extent depends upon the glass transition temperature of polymers. Glass transition temperature (T<sub>g</sub>) is the temperature at which hard glassy. Polymer is converted into a rubbery material. All polymers have higher glass transition temperature and addition of plasticizers reduces the glass transition temperature.<sup>11</sup>

#### 4.1 Oro dispersible films

Orodispersible films (ODFs) are an alternative to fast-dissolving tablets because they possess quality of fast dissolution rate, higher durability and compatibility, and better patient compliance. Because of the following attributes of the orodispersible films they have gain enough attention and interest by researchers even their marketed formulations are also available including Listerine®, Chloraseptic®, Triaminic®, and multivitamins.<sup>12</sup>

Out of those, drug delivery system being very eminent among pediatrics and geriatrics is orally disintegrating films (ODFs). These fast disintegrating films have advantages over fast disintegrating tablets as the latter are associated with the risks of choking and friability. This drug delivery system also has few advantages like they can be used for dysphasic and schizophrenic patients and are taken without water due to their ability to disintegrate within a few seconds releasing medication in mouth. Various methods are employed for formulating ODFs and among which solvent casting and spraying methods are frequently used. Generally, hydrophilic polymers and other excipients are used for preparing ODFs which make films to disintegrate quickly releasing incorporated active pharmaceutical ingredient (API) within seconds. Orally disintegrating films have potential for business due to their enormous benefits over orally disintegrating tablets.<sup>13</sup>

Glycerol, phthalate derivatives like dimethyl, diethyl and dibutyl phthalate, Propylene glycol, low molecular weight PEG,

Citrate derivatives such as tributyl, triethyl, acetyl citrate, triacetin and castor oil are some of the commonly used plasticizers in the concentration of 0–20% w/w of dry polymer weight. However cracking, splitting and peeling of the film might occur with the inappropriate use of plasticizer.<sup>14</sup>

#### 4.2 Glycerol

In various research work it was proved as efficient plasticizer due to its property of changing glass transition temperature and impart flexibility in formulation.

In a research work pullan based oral films were prepared by taking (glycerol, vitamin E TPGS and triacetin as plasticizers). They studied effect of concentrations of plasticizers on physico-mechanical properties of pullulan based oral films. They evaluated prepared films by determining Elastic modulus, tensile strength, elongation at break and disintegration time. The surface morphology of films was evaluated by SEM, while ATR-FTIR was used to determine a molecular level understanding of polymer-plasticizer interactions. The highest elongations were observed in glycerol at 20% w/w. Most of the films disintegrated within one minute without significant differences. In this study they concluded that glycerol is suitable plasticizer compared to others for manufacturing pullulan based oral films.<sup>15</sup>

There are many plasticizers which can be used in oral films because they have been reported as important factors affecting mechanical properties of films. Properties such as tensile strength and elongation could also been improved by the addition of plasticizers. Even variation in their concentration may affect these properties. The commonly used plasticizers are glycerol, dibutylphthalate, and polyethylene glycols etc.

#### 4.3 Poly ethylene glycols

In another study Soluplus® mechanical property was characterized with four different plasticizers. (polyethylene glycol 6, triethyl citrate, propylene glycol, and glycerin) they were studied at three different levels (15%, 20%, and 25% w/w). The effect of these plasticizers on glass transition temperature and mechanical properties like tensile strength, and percent elongation were studied. Young's modulus of free films made from Soluplus® was also measured and the toughness and ratio of tensile strength to Young's modulus were calculated. These results revealed that all four plasticizers are capable enough to plasticize Soluplus® as indicated by the glass transition temperature lowering, tensile strength, and Young's modulus while increasing the percent elongation and film toughness. Among the plasticizers tested, polyethylene glycol 6 showed greatest changed in the mechanical properties studied.<sup>3</sup>

Various studies were carried out in different plasticizers to study their plasticization effect on the gelatin strips, which resulted in observation that malic acid was found to be better plasticizer when compared to citric acid, oleic acid and tartaric acid as it did not crystallize out when the films were dried. Amongst the different grades of polyethylene glycol (PEG); PEG 300 was found to be better plasticizer for gelatin as compared to higher molecular weight PEG. This is because lower molecular weight PEG formed visually superior transparent films and had low water vapour permeation rate. When mannitol and sorbitol were tested as plasticizers for gelatin strips, sorbitol was found to be better as compared to mannitol since it showed the similar problem like that of citric acid. Maltodextrin can also be plasticized and converted into oral dissolving film with incorporation of glycerine and propylene glycol as plasticizer in the concentration range of 16–20% w/w, and found to be more advantageous by using glycerine over propylene glycol as it shows miscibility problems with maltodextrin either by using solvent casting or hot melt extrusion methods. In some cases certain drug molecules themselves can act as plasticizer. For example, Ibuprofen interacted with Eudragit RS 30 D and played the role of a plasticizer. There are two mechanisms propagated of how the plasticization takes place namely internal plasticization (involving chemical interaction) and external plasticizing effect, the latter mechanism is more proffered as it does not involve chemical interactive alterations in the product.<sup>16</sup>

In one another research work initially only film forming polymer were used for the formulation but later on it was combined with the mucoadhesive polymer with plasticizer. This films then characterized by determining swelling index, percentage hydration, erosion of matrix, in vitro release, tensile strength, elongation at break and ex vivo mucoadhesive time. On the basis of the results obtained, the film containing Poly vinyl pyrrolidone and sodium carboxy methyl cellulose and plasticizer poly ethylene glycol was selected best promising film for the delivery of the anti-inflammatory drug.<sup>17</sup>

Sildenafil citrate Fast dissolving films were also developed for oral administration. The films were prepared by solvent casting method by using various grades and concentrations of Hydroxypropyl methyl cellulose polymer namely (HPMC K100, HPMC E4K and HPMC 100). Glycerin and propylene glycol were used as plasticizers for the films. The films were evaluated in respect to their in-vivo & In-vitro disintegration and tensile strength. The time required for 80% of the drug to be released (T80%) and percent drug dissolved in 2 minutes (D2 min (%)) were used for the comparison of the dissolution results. 30 seconds Disintegration time were observed. The result of D2 min (%) and (T80%) for LF4 was 75.56 % and 2.78 min. respectively. At the end the conclusion was drawn out was fast dissolving films were

promising formulation suitable for the immediate release of Sildenafil citrate<sup>18</sup>

#### 4.4 Transdermal films

Transdermal Drug Delivery System (TDDS) are defined as self contained, discrete dosage forms which are also known as “patches”<sup>19, 20</sup> when patches are applied to the skin, It deliver the drug via skin at controlled rate in to the systemic circulation.<sup>21</sup> TDDS are dosage forms designed to deliver a therapeutically effective amount of drug across a patient’s skin.<sup>22</sup>

The main objective of transdermal drug delivery system is to deliver drugs into systemic circulation into the skin through skin at predetermined rate with minimal inter and intra patient variation. Currently transdermal delivery is one of the most promising methods for drug application.<sup>23</sup> It reduces the load that the oral route commonly places on the digestive tract and liver. It increases patient compliances and reduces harmful side effects of a drug caused from temporary over dose.

#### 4.5 Di-n-butylphthalate

A transdermal film was formulate by using different polymers like ethyl cellulose, poly vinyl pyrrolidone and eudragit. Solvent evaporation technique were used for the formulation of twelve formulations of drug free transdermal patches in which each group have different plasticizer concentration and they were evaluated for flatness, tensile strength, folding endurance, moisture content, Water vapor transmission rate and percent elongation. The tensile strength and folding endurance of the patches prepared with 20% Di-n-butylphthalate as plasticizer was high compared to patches prepared by 10% and 15 % Di-n-butylphthalate. The result of 20% plasticizer indicated that the patches would not break and would maintain their integrity with general skin folding when used. All the formulations show 100 % flatness. The WVTR was not significantly affected by varying the concentration of plasticizer (Di-n-butylphthalate). At concentration of 25 % of plasticizer the tensile strength and percent elongation not shows significant result due to soft and sticky formulation. On the basis of above observations we can easily concluded that the Di-n-butylphthalate at concentration 20% of polymers used as plasticizer for further developmental studies.<sup>24</sup>

In other study influence of casting solvent on crystalline ondansetron hydrochloride in transdermal polymeric matrix films which were fabricated using ethyl cellulose and povidone as matrix forming polymers were studied. Different casting solvents like dichloromethane, methanol, chloroform, and mixture of chloroform and ethanol (C-ETH) were used for the fabrication of transdermal films. Di-n-butylphthalate was incorporated as a

plasticizer at a concentration of 30% (w/w) of dry weight of polymers. Analytical tools like scanning electron microscopy (SEM), X-ray diffraction (XRD) studies, differential scanning calorimetry (DSC), etc. were utilized to characterize the crystalline state of ondansetron in the film. The result of analytical tools revealed chloroform as a preferred casting solvent with minimum or practically absence of recrystallization shows relatively amorphous form of ondansetron in transdermal films which is always good for the bioavailability of this formulation.<sup>25</sup>

#### 4.6 Polyethylene 400

In another research work transdermal film was prepared using hydroxypropyl methylcellulose (K15) and carbopol (400) with different ratio of plasticizer (PEG 400) and drug Simvastatin by using film casting method. It was observed that 1% of PEG helped as ideal concentration due to better plasticizing effect. Among all the formulation, HPMC: Carbopol (3:1), polymer concentration with 1% PEG concentration was revealed best release.<sup>26</sup>

Transdermal films of tramadol hydrochloride were prepared to provide the prolonged relief from the severe pain of spinal injuries. Total Six formulations of transdermal films were prepared using three different ratios of sodium carboxymethyl cellulose and Eudragit RS100. Three formulations (T1–T3) contained propylene glycol while other 3 formulations (T4–T6) contained polyethylene glycol 400 as plasticizer and permeation enhancer. The prepared transdermal films were characterized for various physicochemical parameters like moisture content, thickness, folding endurance, tensile strength, moisture uptake, weight variation, scanning electron microscopy and drug content. They concluded that Eudragit and SCMC based transdermal films prepared using PEG as plasticizer can be useful in providing prolonged analgesia in spinal injuries.<sup>27</sup>

Transdermal film of Carvedilol was prepared by the use of solvent evaporation method and combination of different polymers were used such as EC: PVP K-30, EC: HPMC K-15M, EC: Carbopol-934. PEG 400 was used as plasticizers. Film was optimized on the basis of uniformity, folding endurance and transparency. On the basis of physicochemical evaluations and In-vitro drug permeation study, formulation batch A-3 and A-5 were chosen as the best films and among the both preparation, only formulation batch A-5 had maximum permeation, maximum steady state flux and maximum permeability coefficient.<sup>28</sup>

#### 4.7 Dl-limonene

Donepezil matrix type transdermal film was designed to improved patient compliance to Alzheimer disease treatment.

Sodium alginate, a natural polysaccharide, was used as matrix-forming agent in for the optimization of transdermal films. Propylene glycol and dl-limonene were added into films as a permeation enhancer and plasticizer, respectively. Dl-limonene at a concentration of 3% was optimum with high drug flux which was indicated by In vitro skin permeation study indicated. ATR-FTIR results confirmed a more fluidized stratum corneum lipid state in the presence of dl-limonene. Regarding to achieve therapeutic levels of DNP, it seems to be feasible deliver DNP with transdermal films for the management of Alzheimer disease.<sup>29</sup>

#### 4.8 Ocular films

Ocular films are prepared with the objectives of reducing the frequency of administration, improve patient compliance, obtaining controlled release, good instillation of drug and greater therapeutic efficacy in the treatment of eye ailment.

In the research work ocular films were prepared by casting method by using different film forming, mucoadhesive polymers Polyvinyl alcohol and poly acrylic acid and to investigate the effect of different polymers on the mucoadhesive capacity, flexibility and strength of films. Physicochemical parameter like thickness, percent elongation at break, tensile strength and mucoadhesive strength of the films were evaluated to determine its strength flexibility and mucoadhesive capacity. Drug content uniformity and in-vitro release of the formulations were also studied.<sup>30</sup>

#### 4.9 Glycerol and dibutyl phthalate

Ocular films were prepared with the objectives of reducing the frequency of administration, obtaining controlled release, to improve patient compliance good instillation and greater therapeutic efficacy in the treatment of eye disease.

In an research work drug-free ophthalmic films were formed by using different polymers like hydroxypropyl methyl cellulose (HPMC), polyvinyl alcohol (PVA), hydroxypropyl cellulose (HPC), polyvinyl pyrrolidone (PVP), and Eudragit RL 100 polymers in single use as well as in combinations for matrix system design for ocular use and to study the effect of various plasticizers on physicochemical characteristics and permeability of the resultant films. Films were prepared by the solvent casting method on a mercury surface by employing distilled water and ethanol as solvents, and glycerol and dibutyl phthalate as plasticizers. These prepared films were evaluated for weight variation, uniformity of thickness, tensile strength, percentage of elongation at break, folding endurance, hardness, surface pH, and water vapor permeability. Permeability characteristics of these films were studied using Ofloxacin as a model drug. Sterility test was carried out before performing an irritation study on albino

rabbit eyes. There was no sign of any haziness, redness, irritation and swelling in the rabbit's eyes even after 24 hours after removal of the film.

#### 4.10 PEG 400

In the research work ocular film of Timolol Maleate were prepared by casting method by using different film forming , mucoadhesive polymers Polyvinyl alcohol and poly acrylic acid and Glycerin and PEG 400 was used as plasticizers. Effect of different polymers on the mucoadhesive capacity, flexibility and strength of films were also investigated. Mucoadhesive strength, physiochemical parameter like thickness, percent elongation at break and tensile strength of the films were evaluated to determine its strength flexibility and mucoadhesive capacity. Drug content uniformity and in-vitro release of the formulations were also studied.<sup>30</sup>

An erodible ocular films formulation of valacyclovir hydrochloride was developed for the treatment of ocular herpes to enhance therapeutic effect through prolonging contact time with the corneal surface. Films were prepared by solvent casting method using different ratios of polymers HPMC E 15 LV and PVP. PEG was used as plasticizing agent in the formulation The FT-IR studies exhibits no interaction between drug and the polymers. Prepared formulations were evaluated for tensile strength, % elongation at break, surface pH, strain, folding endurance, weight variation, uniformity of thickness, % moisture absorption, drug content, in vitro release, kinetics study, sterility test and eye irritancy test on Rabbit eye. It was observed that with increase in hydrophilic polymer content the mechanical properties and release rate of the films were improved.<sup>31</sup>

Ocular films of drug Naphazoline were prepared and evaluated by film casting method. The evaluation parameters like tensile strength, pH, drug content estimation, weight uniformity, swelling index and in vitro drug release were determined for the selection of optimized film. Films were prepared by using carbopol, guar gum as polymer and glycerin as plasticizer. The in vitro results showed that the release of the drug from F5 batch was 99.12%. F5 batch was found to be best due its better evaluation results.<sup>32</sup>

#### 4.11 Gastro retentive films

Gastroretentive drug delivery is an approach to prolong gastric residence time, there by targeting site specific drug release in the upper gastrointestinal tract for systemic or local effects. Gastroretentive dosage forms remain in the gastric region for long periods and hence significantly prolong the gastric retention time of drugs. Prolonged gastric retention increases the duration of drug

release, bioavailability, reduces drug waste, and could be advantageous for local action in the upper part of the small intestine e.g. treatment of peptic ulcer.<sup>33</sup>

#### 4.12 Glycerin

Gastroretentive mucoadhesive films of captopril were prepared by solvent casting technique by using different types of polymers such as EC, HPMC, and Corbopol, and glycerine as plasticizer. Optimizations of solvent system, plasticizer concentration as well as polymer concentration were done. It was found that the polymer concentration is a potent factor affecting the mucoadhesion strength and drug release of the mucoadhesive gastroretentive films. Prepared gastroretentive mucoadhesive films of captopril was smooth, flexible and good in appearance.<sup>34</sup>

#### 4.13 Polyethylene glycol 400

In one another research work, gastroretentive mucoadhesive based drug delivery system containing Famotidine for controlled release was developed. It consists of a polymeric film loaded with drug and folded into a hard gelatin capsule. After administration film unfolds and its swelling and bioadhesion to the gastric mucosa. Thus by retaining the drug in the gastric region improves its bioavailability. Films were prepared by solvent-casting method using HPMC K4M, Eudragit RLPO and Carbopol 971P NF as polymers and PEG 400 as the plasticizer. The prepared film were evaluated for various parameters such as film thickness, folding endurance, uniformity of weight, surface pH, determination of drug content, moisture content, swelling index, In-vitro mucoadhesive study retention time, *In vitro* unfolding behavior and *In vitro* drug release studies and drug release kinetics. Differential scanning calorimetry revealed there were no polymorphic changes in drug as well as polymers during the formulation of polymeric film. Optimized formulation showed 99.02 % drug release at the end of 12 hrs.<sup>35</sup> In other work which was an effort to develop gastroretentive formulation for controlled drug release of Glipizide using casting technique. Mucoadhesive film was formulated using chitosan and HPMC K4M, PEG 400 was added as plasticizer in film preparation. The film folded in the capsule was shown to unfold and swell under acidic conditions and provide controlled release of drug up to 12 h in acidic medium. According to factorial design films, Nine batches were prepared and evaluated for surface pH, folding endurance, Mucoadhesion force, Drug content, *in vitro* drug release etc, Surface pH of F1 to F9 was In between 6.3 to 6.9 thickness and percent drug content for batch F1 –F9 was found to be in between 0.2 mm to 0.28 mm and 95.4 % respectively . In vitro drug release study of F1 –F9 showed utmost 95 % drug release after 11h. The result indicate that the dosage from is gastro-retentive and can provide controlled release of drugs with narrow therapeutic window.<sup>36</sup>

Table 1: Different formulation prepared by using different plasticizers

Drug	Polymer	Plasticizer	Ref. No.
Simvastatin	HPMC (K15) ,Carbopol	PEG 400	26
Timolol Maleate	Polyvinyl alcohol & poly acrylic acid	Glycerin, PEG 400	30
Famotidine	HPMC K4M, Eudragit , Carbopol 971	PEG 400	34
Glipizide	HPMC K4M,	PEG 400	35
Ambroxol Hcl	HPMC	PEG 4000	37
Amlodipine besylate	Sodium alginate	Glycerine	38
Aripiprazole	HPMC, Maltodextrin	PEG-1000	39
Sertraline	PVA	PEG-400, PG	40
Dexamethasone	HPMC, HPC, MCC		41
Dicyclomine	HPMC, PVA	PEG-400	42
Famotidine	HPMC K15M,	PEG600	43
Piroxicam	Maltodextrin	Glycerol	44
Fentanyl	Polyvinylpyrrolidone	Triethylcitrate	45
Ketorolac	HPMC E15, Na- CMC	PG	46
Levocetirizine Hcl	Sodium alginate	Glycerin	47
Cetirizine Hcl	Pullulan PI-20	PEG 400)	48
Metoclopramide	HPMC E6, Na- CMC	Glycerol	49
Montelukast sodium	Gelatin, MCC, PVP	PEG 400	50
Ondansetron hcl	HPMC	PEG 400	51, 52
Rizatriptan	PVP, Na- CMC	Mannitol	53
Zolmitriptan	HPMC	PG	54
Rofecoxib	HPMC	Glycerine	55
Etophylline	HPMC	Ethylene glycol	56
Ropinirole	Pullulan	PEG 400	57
Tetracycline	Chitosan		58
Domperidone	HPMC E15, HPC	PEG 400	59
Nicotine	Maltodextrin	Glycerol	60
Salbutamol sulfate	HPC	Glycerine	61
Verapamil	HPMC E6, Maltodextrin	Glycerol	62
Dimenhydrinate	Modified pea starch polymer	Glycerol	63
Medicinal carbon	Na- CMC	Mannitol, sorbitol	64
Donezepil Hcl	HPMC	PEG	65
Lidocaine	HPC, HPMC	PolyOx N-80	66
Tianeptine sodium	Lycoat NG73	PG	67

#### 4. CONCLUSION

It could be concluded that from this review that due to the presence of plasticizer all the formulations mentioned shows promising flexibility, mechanical properties, desired characteristics and stability, which modifies the properties of the formulation as stated in different theories of plasticizers. It can also be consider as the vital part of formulations like ocular films, Transdermal films, Buccal films, Orodispersible films, Gastroretentive films, Wound healing polymeric films and many other formulations though Selection of appropriate plasticizer for a formulation is a critical step and various considerations have to be taken. From the above work it could be concluded that plasticizers are important and inseparable part of pharmaceutical formulation but its selection, compatibility and legitimate use are key considerations which must be consider during formulation in order to formulate best formulation.

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