PLASTICS IN CONTAINERS AND EQUIPMENT

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The subject of the symposium at the 1953 meeting of this Conference was "Containers and Closures." At that time Stephenson[1] described some experiences with containers and closures in the pharmaceutical industry. His contribution included many references to the use of plastics as packaging components. Boardman[2] at an earlier symposium on the Storage of Drugs and Medicines also mentioned plastic closures.

In selecting a pack the object is to protect the contents under every condition and in any environment to which the pack may be exposed.

The pack must function efficiently over a wide range of temperature and humidity, be resistant to the effects of light and ageing, have adequate mechanical strength, prevent penetration by liquids and gases (including water vapour), be resistant to mould and insect attack and also be unaffected by the product it contains.

The many plastics which are now available offer to the packer materials with valuable properties which must be known and understood for efficient functional design. Plastics must be regarded as specialised products which should be judged by their established properties and not on superficial appearances. It is essential to realise that familiar names like polystyrene, nylon, polythene and so on, do not refer to clearly defined and standardised products. One name may cover several grades of material each with properties different in degree one from the other. This makes it difficult to give useful quantitative data on the properties of plastics.

For example, transparent tube packs in polystyrene and in cellulose acetate superficially resemble similar tube packs in glass but all three differ radically in gas permeability, resistance to organic liquids and ability to stand heat treatment.

Some of the main uses of plastic components in containers for pharmaceutical products will now be considered.

Closures and Caps

One of the earliest uses of plastics in the packaging of pharmaceutical products was as screw-fitting caps. These are mainly made from phenol-formaldehyde plastics, urea-formaldehyde plastics and more recently, polythene.

The thermosetting phenol-formaldehyde and urea-formaldehyde plastics used for closure manufacture contain fillers the composition of which can materially influence the properties of the finished component. For example, wood filled and paper filled urea plastics show considerable water absorption if exposed to wet or humid conditions, and under fluctuating conditions of temperature and humidity the dimensional changes in a closure made of such material may result in loosening to an extent that leakage or loss of volatile constituents from the container may occur. If, for example, chloroform, which is present as a preservative is lost, secondary deterioration in the form of fungal or bacterial contamination is liable to occur. Alternatively if a closure contracts it may bind on the bottle neck making removal difficult. In extreme cases the physical stress causes the cap to crack. These dimensional changes are particularly undesirable in packs destined for export where considerable climatic variations are often experienced both en route and in the destination. Ordinary wood filled thermo-setting plastics also show poor resistance to alkaline products such as Cream of Magnesia and Aluminium Hydroxide Gel which may cause distortion, cracking and on long exposure disintegration of the closure. By attention to the composition of the moulding powder, thermo-setting plastics can be made which are resistant to alkaline preparations. When purchasing plastic caps for products of the type mentioned it is advisable to specify an alkali resistant grade.

The finish of a plastic cap must be of good quality. It is important that particles of "flash" from the moulding are not present as these may contaminate the product. "Flash" on a black plastic cap used on a container for a white cream or ointment may result in unsightly black specks on the surface. It is equally important that the container itself should be well finished. Pronounced mould marks on a bottle neck or threads may cause abrasion of particles from the plastic closure and in this way contaminate the product. Also, a poor seal may result if the plastic liners, discs or facing are cut.

Most phenol-formaldehyde mouldings can be sterilised by autoclaving but this does not apply to the urea-formaldehyde plastics which can be badly distorted by such treatment. The phenol-formaldehyde plastics are restricted in their colour range and are mostly used as black or dark brown.

Closures for collapsible tubes in thermo-setting plastics are available which make an effective seal without a liner disc or facing. This is achieved by skilful design of the cap moulding and by attention to the shape of the nozzle of the tube itself. Such closures eliminate the nuisance of a small liner disc sticking to the end of the tube and possibly being lost or discarded and also ensure an effective reseal. Wadless polythene caps for eye ointment applicator tubes have been described in the literature and are finding increasing acceptance. Most polythene closures do not use liner discs or secondary seals.

Polythene closures may be either screw-fitting, snap-on, or plug-fitting. With plug closures and snap-on closures the dimensions of the container neck should not vary appreciably. Because of the precision limits to which polystyrene containers can be produced a polystyrene tube closed by a polythene plug is being used for packaging pharmaceuticals such as tablets. In considering such a pack it must be remembered that both polystyrene and polythene are not completely impervious to gases including water vapour and that although for many purposes they afford perfectly adequate protection they do not give it to the same degree as an efficiently sealed glass container. To cope with any slight permeability of the pack to moisture vapour, hollow polythene plugs have been made containing a dessicant such as silica gel granules; the base of the plug is perforated. One such plug is used as the closure for a pack of multi-vitamin pellets. Screw fitting polythene caps are available for winchester bottles, and this pack is in use for concentrated hydrochloric acid.

Many auxilliary closure devices in polythene have been the subject of patent applications. A polythene insert is available which greatly improves the pouring qualities of aqueous preparations from the usual screw necked glass bottle. Our own tests with such a device have shown that it is not so effective with alcoholic or oily products as with aqueous preparations. A similar device on a larger scale is incorporated in at least one well-known make of vacuum flask. Another polythene device which can be inserted in a bottle neck enables drops to be measured with ease and accuracy. This has been used in packaging oily vitamin-containing preparations, the dose of which is measured in drops. A polythene stopper with three flexible prongs has been evolved as a closure for a tube pack of tablets. The tablets are prevented from rattling by the prongs without need of cotton wool or other padding which may act as a reservoir for moisture.

Captive closures moulded as one with the container have been produced in polythene. Reversible spouts in polythene are available for use as a pouring aid from metal drum packs. Many devices of which the above are only a few examples have been described in the patent literature and in the literature on packaging.

Cap Liners

The cap liner is a most important component of a pack because it frequently effects the seal of the container. The use of plastic bonding for composite cork liners gives improved resistance to mould attack which so frequently occurs on composite cork liners bonded with glue of animal origin. Many plastics and plastic laminates find application in cap liners which are widely used under trade names such as Resistol, Crystalcap, Blackol, and Vinylite.

Resistol is paper coated with melamine-formaldehyde resin plasticised with alkyd resin. It is not suitable for strongly alkaline or acid products and is effected by a number of solvents.

Crystalcap is similar in general properties to Resistol but is white in colour this being obtained by pigmentation.

Blackol, which is widely used in pharmacy, consists of paper impregnated with a resin prepared from polymerised cashew nut-shell oil and is coloured with carbon black. It has quite good resistance to acid and alkali and resists some organic solvents but is softened by others. A metal foil liner facing is more satisfactory for solvents.

Vinylite consists of paper coated with white pigmented vinyl acetate, vinyl chloride copolymers. It has good resistance to acid or alkali but poor resistance to organic solvents or heat.

Polythene, polyvinyl chloride and various laminated forms using a plastic film backed by a resilient wad are also in use in cap liners. Polythene and pliofilm are typical plastic materials used as facings for such liners. Pliofilm laminated to paper by a thermoplastic adhesive has low water vapour permeability and is useful as a closure liner for many alcoholic preparations but is unsuitable for oily products. A useful oil resistant film is provided by regenerated cellulose.

Some plastic caps are fitted with liners which are fixed in the cap by adhesive—frequently a plastic based adhesive is used—and with some products the liner may stick to the bottle neck. If this occurs with a faced composite cork wad which is stuck in the cap it is possible on unscrewing the cap to break up the cork backing, resulting in an unsightly appearance and in loss of sealing efficiency on reclosure.

An ingenious polythene cap liner in the form of a plug which fits into the bottle neck has been designed such that when the cap is screwed down, pressure of the cap on the centre of the liner disc forces the sides outwards thus ensuring a really tight closure.

Rigid Containers

Rigid containers fabricated from plastics include bottles, tubes, jars and boxes. The plastics most widely employed for this purpose are polythene, polystyrene and cellulose acetate for bottles and tubes with phenolic and urea formaldehyde plastics also being used for boxes. Nylon bottles have recently been developed which are stated to be capable of repeated sterilisation by autoclaving at 120° C.

Plastic containers have many advantages. They are available in a wide range of colours and opacities and are attractive in appearance; their light weight reduces freight charges and their mechanical durability reduces loss from breakage. The flexibility of a material such as polythene enables many types of container to be fabricated with ease. Offset against the advantages are increased cost compared with containers of glass or metal, together with the greater possibility of chemical or physical actions affecting the contents. Therefore in choosing the plastic container much consideration must be given to the properties of the product and to those of the container.

The increasing uses of plastic bottles has drawn attention to Section 23 (1) (*b*) of the Poisons Rules which specifies that a glass container of capacity not more than 120 fl. oz. used for packing poisons, not being medicines made up ready for internal treatment of human ailments or local anæsthetics for injection in the treatment of human or animal ailments, shall have the outer surface of the bottle fluted vertically with ribs or grooves recognisable by touch. At present this requirement does not apply to plastic bottles. The matter has been referred to the Poisons Board for consideration.

Polystyrene is used to a considerable extent for producing containers by injection moulding. It is a hard rigid material which gives a typical sounding ring when dropped onto a hard surface. It breaks with a sharp fracture and is stable to temperature about 170° F. It is free from odour and taste and is available in a wide range of colours in addition to a transparent finish. It has excellent dimensional stability and components can be produced within fine limits of accuracy. This is important when the closure is a plug as is often the case. Although polystyrene is water proof and has a very low moisture absorption it is not water vapour proof if subjected to varying conditions of humidity and temperature. In the course of work in the author's laboratory to test the suitability of a wide variety of containers for packaging penicillin tablets it was found that polystyrene tubes were very much less satisfactory than glass bottles. By sealing the opening of the polystyrene tube with a cork and dipping in wax and similarly treating glass controls it was shown that after treatment for several weeks in a climatic testing cabinet set to give fluctuating temperatures and humidities over a wide range, the resulting deterioration of the product in the plastic pack was due to water vapour passing through the walls of the polystyrene tube. The pack which was finally chosen to ensure greatest protection to each separate tablet was a strip foil pack in heat-sealing aluminium cellulose acetate laminate, each tablet being hermetically sealed in a separate pocket.

The peculiar properties of polystyrene in transmitting water vapour have been described in the literature[3]. It has been stated that the water resistance of polystyrene is about the same as polythene or polyvinylidine chloride but that the rate of water vapour transmission through polystyrene is incomparably greater than through the other two plastics. The water vapour transmission rate of nylon is also very high.

Polystyrene is not affected by acids, alkalis and alcohols but has poor resistance to chlorinated hydrocarbons and certain organic liquids. Polystyrene is used for one well-known photographic developing tank and has been shown to stand up well to the alkaline solutions used for developers. Polystyrene containers are used for cosmetic products, for example a double shelled jar for creams can be made with a great degree of accuracy and looks very well. Lipstick cases may also be made of polystyrene but these sometimes show surface marking and "crazing" after contact with many essential oils and materials used in perfume.[4]

Polystyrene readily becomes charged with static electricity and attracts to it dust and fibres much more readily than does a glass or metal container. Dusting such containers with a dry cloth merely aggravates the problem. They can be cleaned with a cloth damped with water or with a very dilute solution of a cationic detergent. Antistatic agents are now available for incorporation in plastics including polystyrene. These appreciably reduce the problem of charge. Several years ago the writer observed an incompatibility of plastics—a container was made, the base of polystyrene and the lid from cellulose acetate. After storage for a little time the fine surface finish of the polystyrene base became dulled and pitted and the lid had tightened to such an extent that the container was quite unacceptable. It is possible that the plasticiser in the cellulose acetate reacted with the polystyrene. This effect of plasticisers on plastics is of importance to pharmacists as dimethylphthalate and dibutylphthalate which are widely used in insect repellent preparations are also used in the plastics industry as plasticisers and may soften or dull the surface of plastic articles which come in contact with them. Spectacle frames are particularly vulnerable.

Polythene is used for bottles and tubes and also for collapsible tubes. The bottles can be finished with a variety of separate fitments for delivering a liquid as a spray, as a jet, or as drops; large bottles and containers in sizes up to 50 gallons capacity can be obtained for specialised packaging; puffer containers for powders are also widely employed, and double shell jars are used for cosmetic creams to provide light, unbreakable containers suitable for travelling.

Among the virtues of the material are flexibility, excellent resistance to chemicals (polythene containers have been found suitable for packaging hydrofluoric acid), and low water vapour transmission rates. Although polythene has good resistance to permeation by water vapour it has a relatively high rate of transmission compared with some other plastics, for oxygen, carbon dioxide and many organic vapours. This permeability to gases may result in spoilage of the contents of a polythene container if it is stored with odourous articles, and also the loss of volatile constituents including preservatives from the contents may occur. Pinsky, Nielson and Parliman[5] have carried out a long-term study of 67 chemicals in polythene bottles and have recorded data concerning permeability and physical effects.

Affixing labels by the usual adhesives is unsatisfactory with polythene containers. One useful device on a cylindrical container is to have a recessed panel which will take an all-round band-label stuck to itself. Polythene tubes for pastes and ointments, now beginning to make an appearance in this country, set problems in filling and sealing at speeds comparable with those used for metal tubes. Also on prolonged exposure to sunlight polythene may become oxidised, this gives rise to an odour, and a taste develops which would be imparted to the contents of the container.

Each product must be specifically tested for suitability for packing in plastic tubes. For example, experimental toothpastes packed in polythene were found to lose flavour very quickly, while controls in tin remained perfectly satisfactory.

Bottles of irradiated polythene have been produced on an experimental scale. It is claimed that these can be sterilised with heat[6] as the material does not melt at temperatures up to 350° F. and retains the toughness and flexibility of polythene itself. One possible use for such bottles is as containers for milk, where advantages of lightness and shock-proof qualities apply. The initial cost of the bottles would undoubtedly be higher, but the life of each container longer than its glass counterpart. Facilities for producing containers in irradiated polythene are at present limited.

Transparent polyvinyl chloride has been used to provide an outer safety covering for glass bottles used for pressurised aerosols. Tests have shown that even if the glass bottle bursts the polyvinyl chloride "skin" prevents flying glass. Plastic containers and jars are considerably lighter than their glass counterparts, and when put through conventional bottle-washing machines designed for glass they may be blown off the holders by the jets.

Plastic Films and Laminates

The plastic films most widely used in this country in containers for pharmaceuticals are cellulose acetate, polythene, rubber hydrochloride (pliofilm) and polyvinyl chloride. Other plastic films which are potentially useful but not yet available in quantity in this country include polyvinylidine chloride (Saran), ethyl cellulose and nylon. Regenerated cellulose although not truly a plastic is also used widely as a component of containers.

These plastic films can be used alone or laminated to other materials. Laminates with each other may give a useful combination of properties. Plastic films are frequently employed as components of packs in the form of laminates with non-plastic materials such as paper, aluminium foil, hessian and fibre board. In considering the use of plastic films and laminates as potential containers for pharmaceuticals it is essential to take into account the permeability of the materials to water vapour and gases Riddell[7] has pointed out that, apart from metal foil free from holes, no commonly used flexible packaging material is absolutely vapour proof. Polythene gives good resistance to moisture vapour but has a high transmission rate for oxygen compared with say regenerated cellulose film. Riddell[8] quotes polythene as having approximately 100 times the permeability to oxygen as dry cellulose film of equivalent gauge. In this case, therefore, it might give better product protection to use a moisture-proof cellulose film rather than polythene even though on grounds of water vapour permeability the latter is more efficient.

The films or laminates are used for making bags, liners for drums or sacks and for "sachet" containers for liquids and powders. Polythene liners to metal and fibre board drums enable chemicals to be packaged without actual contact with the outer. The lined drums are free from fibres and foreign bits and provide excellent containers for chemicals required to give "particle free" solutions, and also provide excellent storage and transport containers for soft capsules which in card or fibreboard boxes tend to dull and pick up foreign particles. Many liquid shampoos are packed in plastic or plastic laminated sachets. Materials used for such products include polyvinyl chloride and pliofilm/cellulose acetate laminates where the pliofilm gives good water and water vapour resistance and the cellulose acetate good protection to the perfume. A disadvantage of pliofilm, however, is that it deteriorates with age, particularly if exposed to sunlight, when the film becomes brittle and very readily broken, so destroying the water-resisting barrier which it was intended to provide.

Polyvinyl chloride bags or sachets made of sheet or tubing are in use for a variety of liquid products from horticultural spray concentrates to shampoos. The plastic is readily printed by accepted methods. It is resistant to water and water vapour, it is relatively unaffected by sunlight, has good ageing properties, and is resistant to inorganic chemicals including strong acids and alkalis but is attacked by some organic liquids. Petrols, oils and greases may extract plasticiser and cause embrittlement, however, oil- and grease-resistant grades are available. The material is preferably sealed by high frequency heating, the heat-sealing temperature being in the range 280° to 320° F. (140° to 150° C.).

Many of the thermoplastic films and laminates incorporating them can be sealed or welded by heat. Polythene and pliofilm are readily sealed by heat. Regenerated cellulose is not thermoplastic; the so-called moisture proof heat-sealing variety being dependent on a plastic coating, so there is no true weld, the strength of bond between two sheets being only equal to the strength of adhesion of the coating to the film. In addition to direct pressure heat-sealing, high frequency welding, impulse welding and flame sealing may be applicable according to the properties of the particular plastic film. The optimum temperature range for heat sealing the various plastics is critical. It is important to realise that the actual temperature of the plastic itself must fall within this range and that the temperature of the sealer jaws or plate is no direct indication that this will be achieved. The time of contact with the heated surface and the pressure applied also influence the thermostat setting on the sealing apparatus. A certain amount of experience and trial and error is necessary in establishing optimum settings for a particular piece of equipment. With polythene film, polyvinyl chloride and some other plastics the plastics sometimes stick to the hot sealing jaws. Coating of the jaws with polytetrafluoroethylene eliminates this difficulty. Polytetrafluoroethylene is a good insulator and jaws covered with this material must be applied for two to three times as long as with uncoated jaws to achieve a seal.

Polytetrafluoroethylene is at present very expensive but it is a most interesting plastic. It resists attack by all known solvents and chemicals other than gaseous fluorine and the molten alkali metals. It has anti-adhesive properties which make it useful for coating hoppers and slides on packaging machinery. Bearing surfaces coated with this plastic need no lubricant.

Tapes

The use of self-adhesive tapes on pharmaceutical containers is widespread. Different types of tapes are available according to the properties required. Several are covered by British Standards[9]. Among these are tapes using plastics as the foundation. They include plasticised polyvinyl chloride which gives pliable and extensible characteristics with good resistance to water, oil, acids and alkalis. Polythene based tapes remain pliable, soft and flexible even at very low temperatures. Ethyl cellulose is also used as the base for sealing tapes as also is the widely used non-plastic regenerated cellulose.

Miscellaneous Devices

Miscellaneous devices used in conjunction with pharmaceutical packs include applicators of various sorts. These may be in polythene which is soft and flexible, for example those on tube packs for hæmorrhoidal ointments. Polythene appliator rods are used for corn paints. Plastic measures in polystyrene are used with some products, for example, a spoon is packed with one well known oral penicillin suspension to ensure that the proper dose is given in view of the very considerable variation in the capacity of the domestic teaspoon.

Both nylon and polythene have been used in valves for pressurised aerosol packs.

Platforms and holding devices for irregularly shaped materials are made by vacuum forming from sheet plastic.

Silicone elastomer components are used in order to meet specialised packing requirements where contact with rubber may cause deterioration of the product or where flexibility is required over a wide temperature range.

Plastics in Equipment

Many plastics find application in equipment used in processing or packaging pharmaceuticals. It is not possible to deal with every application of plastics to pharmaceutical equipment and the examples which follow are more direct applications as opposed for example to the use of plastics in electrical equipment used in pharmaceutical machinery. Much the same criteria apply in selecting plastics for use in equipment as apply to their selection for containers. The properties of the plastic must be known in relation to the materials and conditions with which it will come in contact.

Fabrics woven from plastic filaments such as nylon are used for sieves and filter cloths. Microporous polyvinyl chloride sheet provides an excellent filter medium. It is prepared in an ingenious manner by mixing the plastic with starch, casting in sheets and then removing the starch grains by enzymatic digestion to give a porous structure. Polythene funnels and buckets provide non-breakable apparatus for handling corrosive materials. Laminated phenol plastics with fibre have been used for gears in pumps for handling many chemicals corrosive to metal. Similar laminated material has been used to replace teak in carriers used in plating baths where prolonged contact with nitric and other acids is involved.

Amino-formaldehyde plastics are well known under trade names in the form of laminated surfacing for table tops and dispensory benches. They provide a heat resistant, chemical resistant washable surface. Transparent polymethyl methacrylate is used in making dispensing screens for aseptic working. It is also useful in making safety guards on machinery. Tablet counting devices are available embodying polymethyl methacrylate which is also used as a non-splintering alternative to glass in safety goggles and visors.

Plastics in sheet form have been used to line metal equipment where corrosion would result by direct contact with the product. One of the problems in such work is to stick the plastic to the metal, another is the very much greater expansion coefficient of most plastics compared with metal. The temperature at which such lined equipment may be used is limited by the properties of the plastic in relation to heat. With materials such as polythene and polyvinyl chloride extensive areas can be covered by welding several sheets together.

Nylon is used where toughness and durability is of value. On filling machines nylon nozzles reduce the risk of glass chipping which might occur with metal nozzles when a bottle is presented slightly off centre. Engraved nylon face plates have been used in soap stamping machinery. Link chain belting has been made in nylon—it is hard wearing, self lubricating and kinder to glass containers than metal link belting.

The handling of strong solutions of hydrogen peroxide has been helped materially by development of a polyvinyl chloride hose reinforced externally with fabric woven from polyester filaments. Polyvinyl chloride sheets are used for covering pans during manufacture and also for protective aprons. Polytetrafluorethylene has already been mentioned as a facing on heat sealing equipment to prevent sticking of plastic films to the jaws. Due to its very low friction coefficient it is used on feed slides and dough rollers to prevent sticking.

Polythene and polyvinyl chloride piping and tubing find many applications in pharmaceutical plant.

References

1. Stephenson, *J. Pharm. Pharmacol.*, 1953, **5**, 999.
2. Boardman, *ibid.*, 1949, **1**, 931.
3. *Rubber Age and Synthetics*, 1953, 261.
4. *Rubber Age and Synthetics*, 1953, 351.
5. Pinsky, Nielson and Parliman, *Mod. Packaging*, 1954, **28**, 148.
6. *Packaging Review*, 1955, **75**, 53.
7. Riddell, *Chem. Ind.*, 1954, 1570.
8. Riddell, *J. Inst. Packaging*, 1952, **2**, 16.
9. British Standards Institution, B.S., 1133, Sect. 14C/3.
10. *British Plastics*, 1955, 70.