



IMPACT OF SOFT GELATIN CAPSULES FORMULATIONS FOR ORAL ADMINISTRATION

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ABSTRACT

Soft gelatin capsules are also known as soluble elastic or soft elastic capsule. The composition of soft gelatin capsule differs from hard gelatin capsule in that sugar is replaced by a plasticizer like glycerin, sorbitol or a similar polyol. Plasticizers impart elastic properties to capsules. The soft gelatin capsules are hermetically sealed; they are suitable for liquids, volatile drugs and for drugs sensitive to atmospheric oxidation. This has led to the commercial pharmaceutical and nutraceutical industries opting for the development of alternative shell-forming materials instead of the traditional capsule shell material gelatin. This review discusses the establishment and the on-going development of the manufacturing technology for liquid fill capsules with a focus on the progress and challenges of soft gelatin capsules formulation in oral administration for improved solubility and as an absorption-enhancing technique. These considerations form a basis for new applications in oral drug.

KEYWORDS : Softjel, Oral availability, Encapsulated drug, Capsule shell, bioavailability, HPMC.



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INTRODUCTION

Soft capsules are a single-unit solid dosage form, consisting of a liquid or semi-solid fill enveloped by a one piece sealed elastic outer shell. The amount of drug or extract together with adjuvant is enclosed within a globular, oval or other shape of a soft shell¹. Soft gelatin capsules (soft gel) offer the possibility of delivering a liquid in a solid oral dosage form. The soft gel can contain the active ingredient in solution, suspension or emulsion, which will inherently lead to better absorption of the active ingredient as compared with delivery in a tablet or as a powder. Highly developed soft capsules are currently being applied widely in the pharmaceutical, chemical, food and cosmetic industry. This is attributed to the features of soft gels like desirable aesthetic properties and 'swallow ability', safety enclosure, precise contents, and pleasing appearance. This has enabled their use as an effective delivery system for hydrophobic drugs, low melting-point drugs, easy-oxidized drugs, and a variety of health care oil¹. Since the introduction of Soft Capsule Making Machine in the 1970s, formulations have continually become more popular with rapid developments in recent years. This could be illustrated by the emergency of a more than 560 sets of Soft Capsule Making Machine with transfer mode having a production rate of up to 60 billion pills/year (i.e. more than 3600 kinds of drugs) in the world³. Up to now, there are more than 30 manufacturers producing more than 40 kinds of soft capsules by using over 60 sets of advanced machines. Soft gels' ability to enhance bioavailability not only makes them the preferred dosage form of new chemical entities with poor oral bioavailability, they can also be used for reformulation of existing drugs, with the purpose of life-cycle extension.

PROGRESS IN THE SOFT CAPSULE SHELL MATERIAL

Different types of capsule constitutive materials are usually selected for different products. Apart from the traditional gelatin, in recent years new materials have been explored and their application in the development of capsules is progressing rapidly.

Traditionally Used Gelatin Materials

Due to their availability, animal skins and bones have been used extensively as a source of raw material for the formulation of the shell of gelatin capsules. Their excellent film-forming ability and mechanical stability properties of gelatin result in the desired physical properties. Furthermore they can be re-cycled and retain their good performance⁶. The gelatin made from the traditional material like animal skin, bone, tendon and collagen have been noted to meet the necessary pharmaceutical requirements as being quickly hydrolyzed gastrointestinal enzymes. In addition they contain a variety of nutritious amino acids. The purified product so obtained therefore are easily swallowed and rapidly absorbed.

Development New Resources of Raw Materials

In the recent past a number of new sources of raw materials for the gelatin capsule shell have been reported. This range of natural resources like fish to polymers, the fish gelatin has been obtained from fish skin products and formulated as natural hollow capsules of fish oil, spiraling and cellulose. Natural herbal capsules have been reported as concentrated herbal capsules of gold *Lippo* plant capsules. The polymer material Hydroxyl Propyl Methyl Cellulose (HPMC) has also been explored, the odorless, milky, fibrous or granular powder, from linter wood pulp, dissolves completely in cold water but is almost insoluble in ethanol and other organic solvents. FDA has highlighted it as a non-active component that can be used for ophthalmic preparations, oral capsules and suspensions. The gelatin made of hypromellose and pollutant displays chemical stability, friability, low moisture content and oxygen absorption rate.

PROGRESS IN SOFT CAPSULES LIQUID FILL MATERIAL

The formulations of capsule fill have been developed to fulfilling specifications and end-use requirements of the product. Capsulation of liquids that are immiscible with water and non-volatile, such as vegetable oils and vitamin E, have been easily made requiring

little or no formulation. However, solids which are not sufficiently soluble in liquids are reported to be encapsulated as suspensions having a particle size of 80 mesh or finer¹¹. A large group of dietary products are reported to have been commonly capsulated in suspensions form. The two suspension formulation gel production equipment widely utilized domestically is the Chatsworth Machine and the GIC Engineering. Basically all these machines produce soft gels in a similar manner, they have rotating dies and an independent wedge with a pump that control the fill⁷. Filling of soft gel capsules with liquid and semi-solid materials has been successful carried out with selected "fillings" that do not dissolve the gelatin. Liquids that can easily migrate through the gelatin shell, such as water hygroscopic and volatile compounds. Water soluble compounds that may affect the gelatin shell unless they are minor constituents of a formula or combined with a carrier that reduces their effect on the shell. Aldehydes, which have the ability to harden the shell and hence affect its dissolution property. Acidic or alkaline solutions should be avoided, unless they are adjusted to become neutral; acids and alkalis can cause hydrolysis and leakage of the gelatin shell.

Challenges and Opportunities in the Encapsulation of Liquid and Semi-Solid Formulations into Capsules for Oral Administration

The encapsulation of liquids and semi-solids provides solutions for convenient delivery through improved oral absorption of poorly water-soluble drugs. In addition, low dose (content uniformity), highly potent (containment), low melting point drugs, those with a critical stability profile and those for which a delayed release is required are candidates for liquid or semi-solid formulations. Both hard and soft capsules can be considered and in each case the capsule wall may comprise gelatin or some other suitable polymer such as hypromellose. The choice of a hard or soft capsule will depend primarily on the components of the formulation which provides the best absorption characteristics as well as on the physical characteristics, such as the viscosity of the formulation and the temperature at which the product needs to be filled. Numerous

excipients are available for formulation of lipid-based systems and their compatibilities with hard gelatin capsules have been tested. The availability of new enhanced manufacturing equipment has brought new opportunities for liquid-filled hard capsules. Filling and sealing technologies for hard capsules, provides the formulator with the flexibility of developing formulations in-house from small scale, as required for Phase I studies, up to production. Soft capsules are single unit solid dosage forms comprising a liquid or semi-solid fill and are usually oblong or oval in shape. They are formed, filled and sealed in one operation using a rotary die process. The technology is currently available from a few specialist companies. Hard capsules are single unit dosage forms which are manufactured separately and supplied empty for filling. They are always cylindrical in shape, consist of a cap and body and have domed ends. Soft capsules have been used as unit dose containers for liquids for many years whereas hard capsules have conventionally been used for delivery of solids in the form of powders and pellets. Over the last 25 years, new equipment has become available for filling and sealing liquids and semi-solids into hard shell capsules thereby providing a viable option for filling such materials into hard capsules, as opposed to soft capsules. The manufacturing process and characteristics of soft capsules have been adequately reported and will only be included in this manuscript where a comparison to liquid-filled hard capsules is required. This review will focus on the technology associated with the filling and sealing of liquids and semi-solids into hard capsules.

SOFT CAPSULE SEALING & DRUG DEVELOPMENT

Whereas soft gelatin capsules are formed, filled and sealed in one operation, hard gelatin capsules containing liquids or semisolids are filled and sealed sequentially. Different methods have been developed for sealing hard gelatin capsules. The two commonly used industrial methods for sealing of capsules are banding, in which a gelatin band is applied to the overlap between the cap and body of the capsule, and sealing, in which a hydro alcoholic solution is applied to the overlap and the two technologies have been

compared .Both methods are industrially feasible and are described in the General Information section of the USP.To achieve absorption of a poorly water-soluble drug from the GIT requires an innovative formulation approach. Encapsulation of formulations as liquids or semi-solids provides opportunities for delivering such drugs with reproducible absorption and acceptable bioavailability. Low dose or highly potent API, low melting point API and those with a critical stability profile are ideal candidates for encapsulation as liquids or semi-solids in to either soft or hard capsules. Additional opportunities offered by the hard capsule include the option of using laboratory scale equipment in-house to manufacture small batches for stability and clinical trial purposes in the early stages of drug development during which API supply is usually limited. The filling and sealing of liquids and semi-solids in to hard capsules has a significant advantage over soft capsule manufacture: on the one hand there is no need for a time consuming gel mass preparation because empty hard capsules are ready for use; on the other hand the time taken from capsule filling to packaging of the filled sealed capsules only takes from 6 to 12 h. Soft capsule manufacture due to gel mass preparation and the time consuming drying process may last from 2 to 5 days. During soft capsule forming, the gelatin films contain a significant amount of water and there is a high potential for water to migrate into the fill and for components of the fill to migrate into the soft capsule shell. Hard gelatin capsules have a controlled and significantly lower moisture level which may be lowered further to limit possible water exchange with the fill. However, as with any process, the filling of liquids and semisolids into capsules also

presents challenges to the formulation scientist. The stability of an API in a liquid dosage form, as opposed to a solid dosage form is, in itself, a challenge, as is matching the formulation with the characteristics of the capsule shell and the dosing system of the capsule-filling machine. In cases where gelatin as a capsule material is not suitable, alternative polymers for capsule production are available.

CONCLUSION

To achieve absorption of a poorly water-soluble drug from the GIT requires an innovative formulation approach. Soft gelatin capsules are numbered according to their capacity in minims.Normally the soft gelatin capsules are in different sizesto contain form 0.1 to 30 ml volume.Their additives are added to according to nature of drug.. Additional opportunities offered by the hard capsule include the option of using laboratory scale equipment in-house to manufacture small batches for stability and clinical trial purposes in the early stages of drug development during which API supply is usually limited. The filling and sealing of liquids and semi-solids in to hard capsules has a significant advantage over soft capsule manufacture: on the one hand there is no need for a time consuming gel mass preparation because empty hard capsules are ready for use; on the other hand the time taken from capsule filling to packaging of the filled sealed capsules only takes from 6 to 12 h. Soft capsule manufacture due to gel mass preparation and the time consuming drying process may last from 2 to 5 days.

REFERENCE

1. Ansel Pharmaceutical dosage forms- Edition 7th ,Page No.237,
2. Pharmaceutical practice &Technicians-Durgin & Hannis -5th,Page No.45,Vol.I
3. Development of Solid oral dosage forms-William-Rorter,ThirdEdition,Page No.201,Vol.II
4. Hand book of Pharmaceutical formulations-K.Niazi,First Edition,Page No.26(1),Vol.I
5. Design & Manufacture of Capsules-Aulton SecondEdition,Page No.452,Vol.II
6. ATextbook of Liquid filled capsule dosage forms- Mangesh Bhutkar, Dr Adhikrao Yadav,First Edition,Page No.320,Vol.III

7. Polymer capsules by Fundan, First Edition, Page No.132, Vol.I
8. Bipharmaceutics&Pharmacokinetics- Venkateshwarlu–CBS Publisher, Second edition, Page no.166, Vol.II
9. Hand book of capsule formulations- Kasture Vadokar, Page no.142, Vol.II, 3 edition.
10. Capsules development studies by BK.Gupta, Page no.325, Vol.II, Fourth edition.
11. Pharmaceutical capsules-2nd Edition, Page no.14-10, Vol.I
12. A Text book of Pharmaceutical studies by Lachman, Special edition 2009, Page no.375