OBSERVERSHIP REPORT

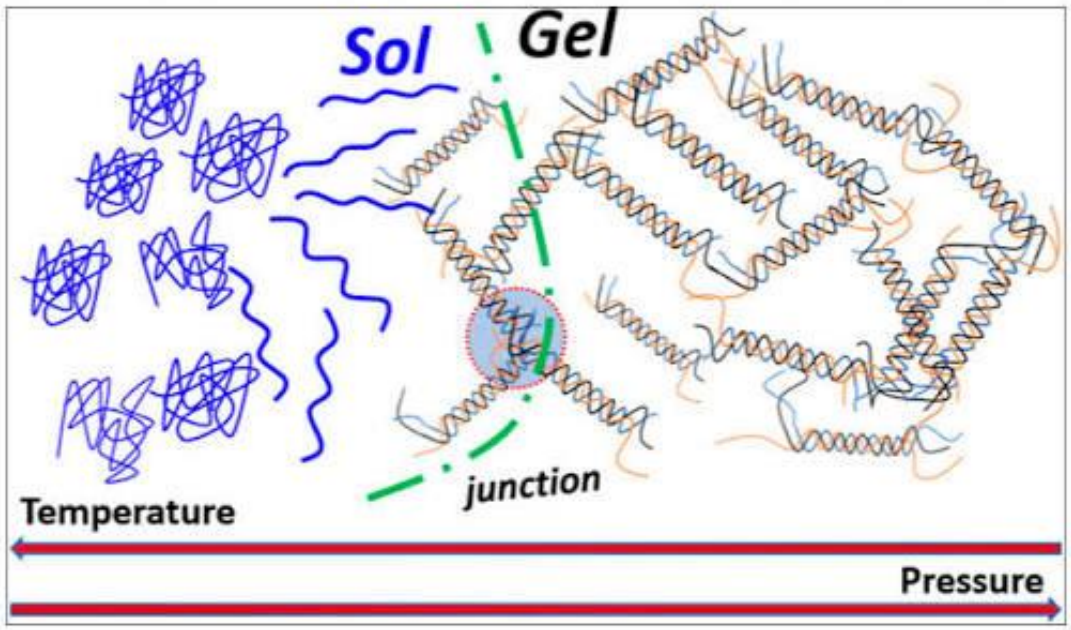
Manufacture of empty hard gelatin capsule shells — Bio-Caps India Ltd, Dankuni, West Bengal

I visited the Bio-Caps India Ltd factory, a producer of empty hard gelatin capsule shells to Indian Pharmacopoeia standards, and was shown the full route from gelatin solution to packed capsules along with the quality-control and microbiology laboratories. The plant makes capsule sizes 00 to 4 and also offers vegetarian HPMC, preservative-free and TSE/BSE-free capsules. This report focuses on the chemistry behind what I saw.

The chemistry of gelatin

Gelatin is a protein made by the partial hydrolysis of collagen. Acid or alkali treatment followed by hot-water extraction breaks the hydrogen bonds and some cross-links of the collagen triple helix, giving single chains that dissolve in warm water and set to a gel on cooling. About one residue in three is glycine, in a repeating Gly-X-Y pattern where X is often proline and Y often hydroxyproline; the small glycine lets the chains pack tightly and hydroxyproline hydrogen-bonds to stabilise the helix. Capsule shells need gelatin of high bloom strength (a measure of gel firmness) so the thin film picked up on the pins sets fast and holds its shape.

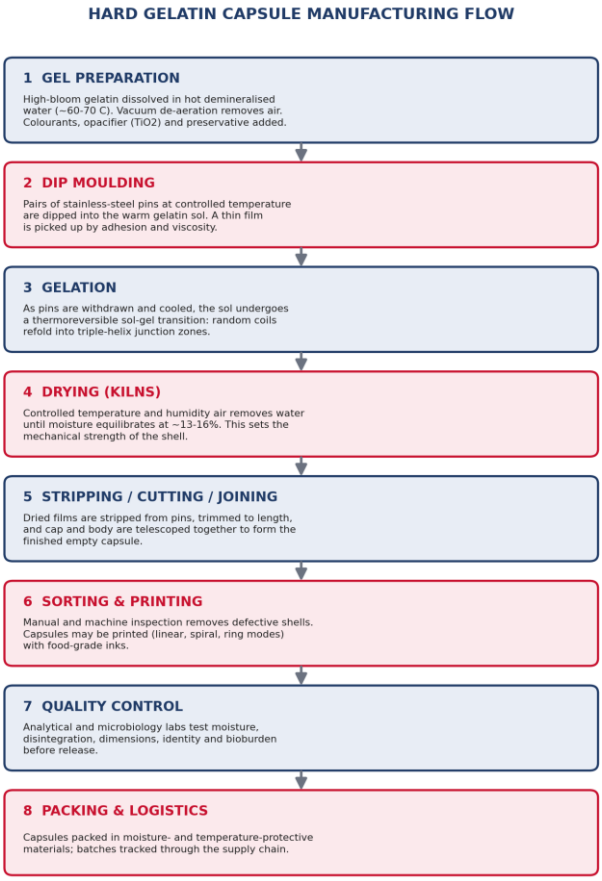
The key property for manufacture is the thermoreversible sol–gel transition. Above about 35 °C gelatin is a liquid sol of random coils. On cooling, sections of the chains refold into short triple helices that act as junction zones, linking the chains into a network so the liquid sets. Gentle reheating melts these helices back to a sol. No chemical reaction occurs, only physical cross-links forming and breaking, which is why a warm sol can be picked up on a cool pin, set at once, and then dried.



The thermoreversible sol–gel

The manufacturing process

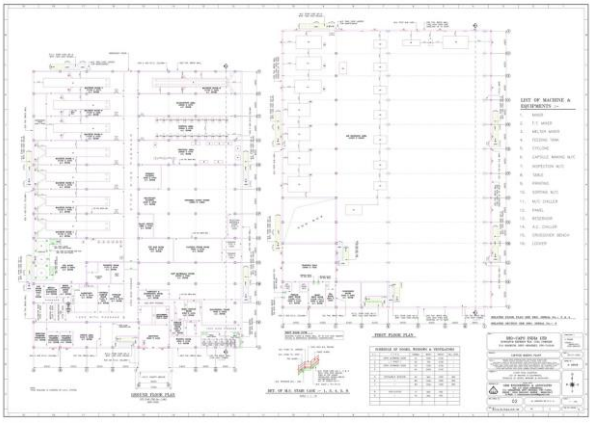
Capsules are made by dip moulding. Gelatin is dissolved in hot demineralised water (~60–70 °C) and held under vacuum to remove air; colourants, opacifier and preservative are added and viscosity is set. Cap and body pins are dipped into the warm sol, the film gels as they cool, and the coated pins are dried in kilns until moisture equilibrates at about 13–16 percent. Water acts as a plasticiser, so too little makes the shell brittle and too much makes it soft; controlling drying humidity therefore controls quality. The dried shells are stripped, cut to length and joined, then inspected, optionally printed, and packed in moisture-protective materials.



Flow of the hard gelatin capsule process observed during the visit.

Quality-control chemistry

The quality department has separate analytical and microbiology laboratories. Moisture is measured on every batch by loss on drying or by Karl Fischer titration, which is specific to water through its reaction with iodine and sulfur dioxide. Disintegration is tested in water at 37 °C, where the warm water melts the gel network. Viscosity and pH of the gel solution are checked during preparation, and microbial counts are run using an incubator and an autoclave. HPMC (vegetarian) capsules differ chemically: hydroxypropyl methylcellulose is a cellulose ether that gels on heating with a gelling agent such as carrageenan, and it resists brittleness at low humidity.



The analytical laboratory: balances, pH meter, drying oven and glassware.

What I learned

The visit showed how one well-understood polymer becomes a precise pharmaceutical product through control of physical chemistry rather than dramatic reactions. Almost everything rests on one reversible change, the sol–gel transition, and on the control of water, so a few percent of moisture and a few degrees of temperature separate a good capsule from a defective one. Recognising techniques such as loss on drying and titration in practice connected my classroom chemistry to industry and strengthened my interest in chemistry and chemical engineering.

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