Transcript for “Fill me in”

Nigel Langley: So, hi everyone, my name is Nigel Langley, I'm the Global Technology Director for BASF Pharma Solutions. And I'm also hosting a series of podcasts of which one is today and it gives me great pleasure to be here to introduce a podcast based on softgels in the pharmaceutical industry.

And with that, I have a very special guest, Lindsay, who I will ask Lindsay to introduce herself to you and then after that we will get involved [00:00:30] in the conversation. So Lindsay, now, can you give us a little bit more background to you, to yourself and what you do?

Lindsay Johnson: Yes, thank you so much, Nigel, for having me here today. My name is Lindsay Johnson, I'm the Global Technical Marketing Manager for the Solubilization Platform in BASF Pharma Solutions. Within that, I'm responsible for the commercial and technical campaigns and support of especially efforts around solubilization techniques in oral and parenteral dosage [00:01:00] forms, including softgels which we'll discuss today. So I really appreciate you having me, thank you.

Nigel Langley: Thank you very much, Lindsay, that's a very nice introduction. And so what is, what is the relevance of softgels in the pharmaceutical industry? Why is it an important technology and why do companies actually develop their drug products in soft gels? Can you elaborate a little bit on that?

Lindsay Johnson: Yeah, sure. So softgels have a number of solubilizing and processing [00:01:30] advantages in a lot of ways over some other oral dosage forms, which makes them especially ideal for some formulations. So, for example, softgels deliver a liquid matrix that is designed to solubilize the active and it delivers that liquid matrix at the same time that it's delivering the active that goes along with it.

Softgels have a very nice CMC profile [00:02:00] to them, so you can load them with precise concentration of an API. So for example, for a highly potent drug, softgels have the advantage of repeatability, for a low dose drug, they have the advantage of precision filling, things in this realm. So very reliable for any sort of unit dose for softgels.

They also, as you think of OTC products that are softgels, one of the key [00:02:30] advantages of softgels is the rapid onset of action, right? Fast acting NSAIDS, for example, are typically formulated as a softgel, so that brings an advantage, you know, obviously in any sense that a softgel is used in that way.

And softgels, really, they offer a lot of the same advantages as tableting. So you have taste masking, odor masking potential for softgels you have an easy platform to provide protection [00:03:00] from air and light and I would say one of the biggest advantages that softgel has over some other conventional tableting methods would be the limited stress on the excipient and the API during manufacturing, you don't have the thermal stress, you don't have the local kinetic stress of extrusion, things like that.

Nigel Langley: Wow, that's great, that's a nice picture that you presented there of what softgels are doing. I guess [00:03:30] softgels means soft gelatin capsules is that, is really that's captured and ... But my understanding is there's alternatives now not just to the gelatin. Can you elaborate a little bit on some of the alternatives that might becoming through?

Lindsay Johnson: There are, there are. You know, softgels as a terminology, comes from soft gelatin capsules. But just as you said, there's a market expanding in the direction of vegetarian capsule, films that can be used for the same [00:04:00] type of final dosage form. You have sort of plant-based polysaccharides that can be used in this realm.

This really helps expand into vegan and vegetarian markets, whereas gelatin is obviously animal-derived and had that limitation when going to market. But there's a developing variety available to soft capsules [00:04:30] even eliminating that middle word of gelatin.

Nigel Langley: Okay. But you, probably fair to say that the majority of products still developed in the pharmaceutical area are based on soft, on gelatin as a substrate, is that correct?

Lindsay Johnson: Of course it still has the nice blooming properties upon action, it still has really favorable mechanical properties to the film itself. It provides ... It's impermeable to oxygen and [00:05:00] so in that sense it provides that inherent benefit to protecting the API. So for the dominating film right now, we are still using gelatin.

Nigel Langley: Okay, very good, thank you. And so let's take a look, maybe, in the fill part, right? So you've got a soft gelatin, or the gelatin is the as the cover if you like, or the external part to the softgel capsule. But, what about the, this film? And can you talk a little bit how, you know, the API and the excipients play a role [00:05:30] here?

Lindsay Johnson: Sure, so, you know, obviously as an excipient supplier, BASF has a wide range of chemistries that are available for soft gelatin pills. Softgels and fills are conventionally going to be oils. So you've got some corn oils in the market,

you've got castor oils. There'll also be, for example, triglycerides. We have, you know MCT 70 in our portfolio, triglycerides are important.

You also have [00:06:00] ethoxylated castor oil derivatives that can be used in softgels and capsules. And then, obviously you have the PEGs. You have polyethylene glycol. Those are very common to soft gelatin capsules although I will sort of share with especially PEGs, these are notorious chemistries for aldehyde content. And in the soft gelatin system, that aldehyde can [00:06:30] provoke cross linking of the shell and really disrupt dissolution.

So if you're looking at especially PEGs, low molecular weight PEGs, you're going to want to start with a low aldehyde grade in order to ensure dissolution stability over storage.

Nigel Langley: Okay, that's an interesting point. So, within the excipient area, you have some requirements on the quality of the raw materials that are going into the softgel side, so that's interesting [00:07:00] for our listeners to understand that, I think.

If maybe we can turn to, our thoughts towards poorly soluble drugs, which have its own, their own inherent challenges for formulators don't they? And so would you think that the softgel, um, capsule approach would be a preferred technology, at least initially to formulate some of these very poorly soluble drugs, especially if they're lipid based poorly soluble drugs?

Lindsay Johnson: Yeah, of course. We [00:07:30] often think of the distribution of pharmaceuticals as preferring tablets, but for poorly soluble drugs, the easy tableting methods, for example, like direct compression, aren't necessarily suited for poorly soluble drugs that have to undergo amorphization, or they have to be stabilized through an excipient-drug interaction, or something like this.

So, softgels provide a great [00:08:00] starting platform for a formulation based on a poorly soluble drug. And we've shown, for example, that our crystallization inhibitors can be loaded into PEG at, you know, 40 weight percent loading, which is fantastic, and provides a lot of opportunities for stabilization against crystallization in storage.

We have also shown a number of self-emulsifying drugs delivery system formulations that we can start from that are perfectly suited for [00:08:30] a soft gelatin capsule in general. And self-emulsifying drug delivery systems bring that extra advantage of improving bioavailability. You're not just fighting crystallization, but you're actually creating a spontaneous emulsion that can improve that absorption through your GIT tract.

Nigel Langley: Okay, that's fascinating. Yeah, so softgels present an opportunity, as you mentioned, to formulate these very difficult [00:09:00] molecules, so small molecules to formulate with.

So you can control their release kinetics as well during that process or are there other means to actually control or adjust the release, say, for example, can softgel capsules be coated with different types of polymers?

Lindsay Johnson: Yes, of course. We've got enteric release polymers that can be coated onto gelatin capsules very akin to how you would for a tablet. [00:09:30] You can coat a softgel for a number of reasons. You can coat it to modify release, you can coat softgels and capsules to provide an opacity to protect against light. You can coat softgels and capsules for ease of swallowing and we have chemistries available for all of these potential needs should you be interested in a sort of a coated application.

Nigel Langley: Oh, that's great. I'm thinking through this though, that, you obviously talked about [00:10:00] the advantages and some of the reasons why you would use types of excipients. You've got fills, liquid fills, you have the self-emulsifying drug delivery systems, a formulated system, especially around poorly water-soluble drugs.

But, you know, softgels is only one technology compared to tablets. You mentioned that people tend to gravitate normally towards tablets. Are there reasons behind that? Is it not because [00:10:30] this technology's not readily available through the industry, or is it, just available in certain areas?

Lindsay Johnson: So I would say at the bench lab scale, there's a limitation in ease of early development for softgels in this way. So you're typically going to have a formulation. And pretty early in your formulation process, in your development process, you're likely going to need to partner with [00:11:00] an external CDMO or CMO that specializes in softgels.

And I think that might be intimidating in some ways, although, it really shouldn't be, because there are great partners out there that are available, that are happy to help with that scale-up process. And once you have that initial scale-up step taken, further scale-up is even quite easy because as you go to higher volumes of a soft gelatin [00:11:30] production, it's relatively the same mechanism. You don't have to go to different sprayers or you don't have to go to different tableting machines. And, so the hurdle is more up front, but I think overall there's an easier development pipeline in some cases.

Nigel Langley: Perfect. And what do you see innovation-wise going forward with this type of technology? Is there still opportunities to improve [00:12:00] or to increase the opportunity with this type of technology or are we done now?

Lindsay Johnson: (laughs) I don't think we're ever done with innovation. We're seeing some, we're seeing some trends that follow tablets, for example TiO2-free opaque capsules, for example, is a relatively new innovation that's coming forward. There's also some pretty [00:12:30] interesting designs where you have a tablet in a capsule and in that case you're delivering either, maybe, the liquid fill helps the tablets release the drug appropriately or you have multiple APIs in different systems, so it's, sort of, a combination therapy through two avenues at once. There's some really interesting concepts coming through the market right now.

Nigel Langley: Yeah, that sounds great. And [00:13:00] so it's got utility and it's also a technology that's not going away fast.

Lindsay Johnson: No.

Nigel Langley: There's lots of other things that we can do with this and companies are actively and obviously developing innovation in this area, that's super. Thank you Lindsay, for your insights here and it's been a pleasure talking to you today. And I think our listeners hopefully have, understand a little bit more about softgels and the importance that they play in the industry. And with that I thank you very much [00:13:30] for your attention and look forward to the next podcast, there's one just around the corner. Thank you -

Lindsay Johnson: Thank you Nigel.