

Transcript for “Influence of excipients on dermal drug delivery.”

Nigel Langley: In the next minute, 250 babies will be born to add to the world's population. In the next 30 years, the world population is expected to reach 10 billion people. These are the 10 billion reasons we do what we do every day. Please join us as we explore innovative pharmaceutical solutions and sustainability and digitalization initiatives that will help us rise to the challenge.

Hi, everyone, my name is Nigel Langley and welcome to 10 Billion Reasons, the latest in our podcast series. And today's topic is dermal drug delivery. And with me today and a great pleasure to have two experts in this field, Gloria and Norm. And I'll ask them each now to introduce themselves. So, Gloria, would you like to introduce yourself first?

Gloria Ho: Sure. Thank you so much for having me today. My name is Gloria Ho, I'm the Global Technical Marketing Manager for BASF Pharma Solutions, specifically for their topicals platform. I joined BASF back in 2018, after graduating with my doctorate in pharmacy. And prior to that, I had specialized, within the personal care industry,

Specifically focusing on cosmetic formulation development in addition to fragrance toxicology. And furthermore, I do have a background in, topical and ophthalmic formulation development. So I'm so glad to be able to be here today. Thank you.

Nigel Langley: Thank you, Gloria. That's great. And, Norm, would you like to introduce yourself as well.

Norman Richards...: Sure, Nigel Norman Richardson. I'm Technical Services Manager with BASF Pharma Solutions servicing North America. I've been 10 years with, BASF. And, actually starting, so long ago as 1988, I've been working on topical products. I worked with Unilever, Pfizer, Johnson & Johnson. And I've spent most of my 10 years at, BASF supporting topical product developers.

Nigel Langley: Thank you, Norman. It's a great pleasure to be with two experts in this field. And maybe what I can do is to start with a question with, with my and Gloria about, in this dermal drug delivery, you know, why does the skin pose such a challenge to dermal drug delivery?

Gloria Ho: Sure. I think that's a really great question. As the largest organ on the body, the skin plays a very important role in really protecting the body from mycotoxins or really exterior substances. And while it is great at also regulating our body temperature, unfortunately, the skin also plays a role in keeping desirable materials out of the body as well. Some of these desirable materials would be

considered, for example, active pharmaceutical ingredients or drugs that would be used to really treat different kinds of, ailments or, or diseases within the body. So unfortunately, while it is great in certain instances, the skin does pose a challenge for formulators.

Nigel Langley: So you would, would you say, Norman, that, that that's the role of excipients in this area then to actually, allow the passage of APIs through the skin barrier? And if so, how, how, what is that challenge specifically? What type of excipient do you need, to actually address that, that barrier?

Norman Richards...: Well, specifically, I would say it's the role of a class of excipients that we call permeation enhancers, right? So, permeation is the objective. You want to get the active through the outermost layer of the skin where the most intensive, barrier properties are. And you want to get into the living tissues of the skin or even into the bloodstream to go systemic or to the joint that you might be treating for pain, right? But you need it to get it through the skin. So, it must permeate. So, we talk about permeation enhancers. These are excipients that when you have them in the formulation, they have an effect on the skin such that you can increase the diffusion rate through the skin and drive molecules, more quickly and effectively through the skin barrier.

Nigel Langley: Thank you, Norman. And, and, Gloria, could, would, would you like to add to that picture on what these types of skin permeation or skin penetration an-answers might be and what type of, excipients are they typically?

Gloria Ho: Sure. So when we think about these, permeation or penetration enhancers, there's quite a few different chemistries which are employed for this purpose. For example you may see alcohol, sulfoxides, glycols, terpenes, amides, fatty acids, ether alcohol, surfactants, pyrrolidone's, or even esters really used for this purpose.

And for each of these specific kinds of chemistries, the way in which you really determine which one is suitable is also dependent on that compatibility between that permeation enhancer with the active pharmaceutical ingredient in addition to the other excipients that are going to be used within the formulation.

So, when we really think about these permeation enhancers, there is a lot to really consider to be able to make that correct decision. And at the same time, really limit any of those side effects that could result from trying to, , improve the permeation of that drug through the skin.

Nigel Langley: Excellent. Thank you for that. That's, that's great information. And, and, Norm, how do the, skin permeation enhancers actually work? What's the mechanism?

Norman Richardson: Yeah, so look, before I answer that, look, it's good to think about the microanatomy of the stratum corneum which is the outermost layer of the skin,

which really presents the greatest barrier. And, and some people have likened that to like a brick wall. It's this brick-and-mortar model. So, you have dried flat cells called corneocytes that are stacked together and interlocked. And between those cells you have a lot of lipids that is very organized. So, you have a lot of structure, a lot of microstructures. And this exact arrangement, is difficult to penetrate.

So, it takes a long time for a molecule to be able to get through or to not even to get it through at all. So the penetration enhancers, a majority of the materials that we consider penetration enhancers for topical drug products, can penetrate, these are molecules that can penetrate into the stratum corneum and they can change the arrangement of the lipids. They can make lipids that are rigid. They can make them fluid. ultimately, by a number of different ways, it could be fluidization, it could be actually dissolving, it could be creating spaces in the lipid domains. Ultimately, what you're doing there is you're shortening the pathway through the stratum corneum.

Nigel Langley: Okay. And very interesting, Norman. And is, is this once the pathway has been shortened then is the excipient then has its use? does the stratum corneum just re- go back to where it was before? Does that-

Norman Richardson.: Well, Ideally-

Norman Richardson: Ideally, the permeation enhancer that you're using, you want that to, leave the stratum corneum and to permeate and not to, compromise the barrier permanently, obviously. So that would be one of the important attributes of a, a safe and effective permeation enhancer.

Nigel Langley: Hmm. I would also imagine, I guess, if you've got highly compromised skin, if you're looking at skin diseases for an example that, would that determine which type of excipient, permeator or penetrator that you would use?

Norman Richardson: Most definitely. So first of all, if you have compromised skin, you may not even need a penetration enhancer because you have a lot of the living tissue is exposed, so the stratum corneum is not normal. So, the barrier is broken. But if you are going to use a formulation that has a penetration enhancer, just like any other ingredient in that formulation, you want to make sure that it's mild and, and non-irritating.

Nigel Langley: And with that, Gloria, maybe you can expand a little bit, if you may, you know, what, how is the selection process, given, let's have the case of intact skin, a normal person's skin, rather than compromised? How would you actually select the ideal skin permeator or penetrator?

Gloria Ho: Sure. So that's a great question. So, when it comes to selecting the ideal permeation enhancer, unfortunately, this really isn't a one-size-fits-all solution. Typically, what we would do, particularly in that kind of lab environment, we will look at multiple permeation enhancers which could be possible candidates. To determine that list of candidates, we'll first select based off of compatibility between the excipient, between the other excipients that would be used in the formulation in addition to the API of interest, in conjunction with that permeation enhancer of interest. Next, after we determine that there shouldn't be any incompatibilities, we will formulate them together and then, we will have the material tested for long-term stability to see that it doesn't really result in any kind of incompatibilities in the long run or any instability issues, for example, reduction of the viscosity, or anything really within that kind of space.

Stability studies will usually involve microstructure. In addition, we are also able to conduct diffusion studies in which we will run, these kinds of formulations through a front cell, , to run these IVRT or IVPT studies, in which case we can determine, which permeation enhancer does offer the best effect; whether it's, deposition within the epidermis or the dermis of the skin, or really having the active ingredient permeate all the way through into really the bloodstream to get more a systemic fact.

It would really depend on what the targeted application of the product would be. And then finally, what we will do is when it comes to these products, we are also interested in the mildness in addition to the sensory profile of that permeation enhancer. In the ideal case scenario, in addition to offering that safety and effective profile, what we also want is to make sure that the finished product is something that a patient would be willing to use, it's cosmetically acceptable, so that we can guarantee or at least promote long-term patient compliance and acceptance.

Nigel Langley: Thank you, Gloria, for a very extensive discussion point and answer to that question. And we're coming towards the end of the podcast now and I just want to ask you, Norm, if you can maybe summarize the key characteristics that are, that an ex- ideal skin permeation or penetration enhancer should possess.

Norman Richardson: Well, so one is that it should be a good solubilizer of the API. So, if the API is not soluble in that material, then you're not going to have a good penetration effect. It needs to be mild and safe, which Gloria has already mentioned, that's critical. It needs to be able to penetrate into the skin to exert an effect in the skin, right? So, if it can't penetrate into the stratum corneum, it's not going to be changing any properties and helping with the enhancement. And it needs to be something that can migrate out of the stratum corneum also. So, these would be the key features. Obviously, it has to be something that's a, a fluid at room temperature and at skin temperature. That would be critical too for its usefulness. Yeah.

Nigel Langley:

So, a lot to consider then as, as a formulator, I guess, on the s- on the selection a and the type of excipient that's used. Thank you very much, , Gloria and, and Norman. That completes our podcast today and our 10 Billion Reasons series. And with that, I thank you very much for your attention. Please listen in to our next podcast, , that would appear soon. Thank you again.

Speaker 4:

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