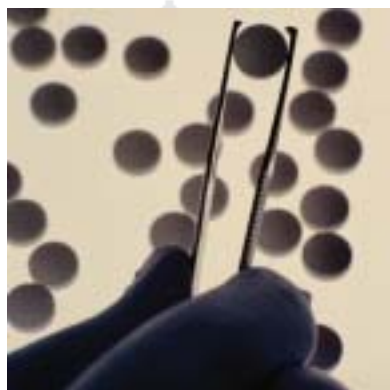


Behavior of Uptake of Moisture by Drugs and Excipients

under Accelerated Conditions of Temperature and Humidity in the Absence and the Presence of Light

Part III: Various Drug Substances and Excipients

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The influence of light on the rate of moisture gain was investigated in 36 drug substances and 18 excipients. The light caused accelerated moisture gain only in hygroscopic drug substances and excipients, and the magnitude of acceleration was greater for the drug substances than for the excipients.

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Recently, we reported that light accelerates the rate of moisture gain by a hygroscopic drug, ethambutol (1). This physical phenomenon was observed when ethambutol and its combinations with other antituberculosis drugs were subjected to stability studies in chambers set at 40 °C and 75% relative humidity (RH) in the absence and the presence of light. The study was later extended to packed and unpacked marketed antituberculosis products to determine whether those formulations also exhibited different behavior in the absence and the presence of light. The same phenomenon was found to occur in the case of even unpacked and blister-packed products (2).

In the meantime, a study was also undertaken to determine whether this phenomenon was applicable, in general, to other drug substances and excipients. For the study, 54 pure drug substances and excipients were exposed to accelerated conditions of 40 °C and 75% RH in the absence and the presence of light. The results are presented in this article.

Experimental

Materials and methods. Thirty-six pure drug substances and 18 pure excipients were sourced from local manufacturers or suppliers. These were used without any purification or treatment. A 100-mg quantity of each was weighed and subjected to accelerated conditions of temperature and humidity (40 °C ± 1 °C and 75% RH ± 3%) in dark and light chambers, using the same equipment and methodology as in our previous studies (1,2). Because a large number of drug substances and excipients were involved in this study, the initial investigations were made once. In cases where some influence of light was observed, a repeat study was carried out in triplicate.

Results and discussion

Figure 1 shows the profiles of moisture gain in the absence and the presence of light for known hygroscopic drug substances. Figure 2 shows the typical behavior of a few nonhygroscopic

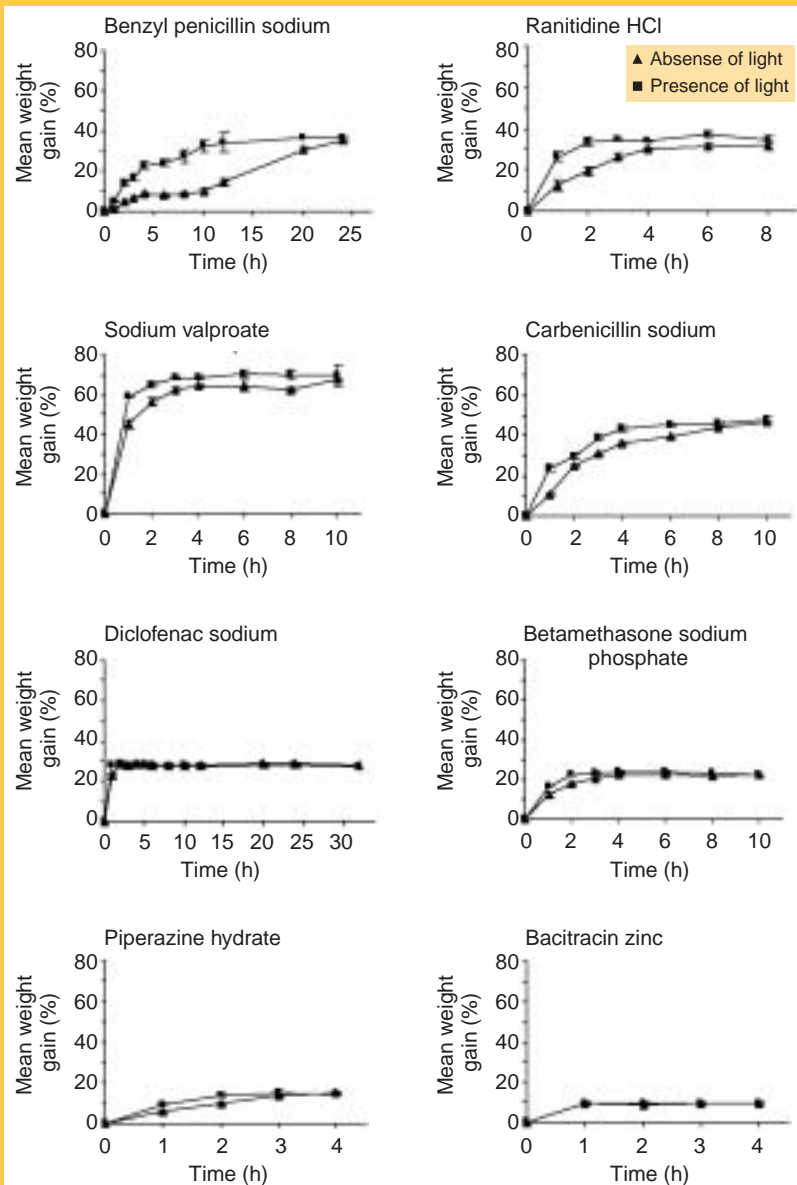


Figure 1: Moisture gain behavior of known hygroscopic drug substances in the absence and the presence of light.

drug materials. Figure 3 shows the profiles of 10 excipients in which the rate of moisture gain was enhanced in the presence of light. Light did not affect the other excipients, and their profiles in the absence and the presence of light were similar to those shown in Figure 2.

The profiles shown in Figures 1–3 provide sufficient evidence that the phenomenon of accelerated moisture gain in the presence of light occurs widely among hygroscopic drugs and excipients. The profiles indicate that light is unable to induce hygroscopicity in drugs and excipients and only influences the rate of moisture gain of hygroscopic materials. The Figures also show that the differences are observed only at early time points; there is no change in the total moisture uptake at equilibrium, which is reached in < 24 h.

Figure 1 shows that the influence of light on the rate of moisture gain by hygroscopic drug substances varies widely, from nil to substantial. Diclofenac sodium and bacitracin zinc are two clear examples in which no influence exists. Piperazine hydrate and betamethasone sodium phosphate show only a small influence, whereas ranitidine hydrochloride, sodium valproate, and carbenicillin sodium show a greater degree of influence. The maximum difference in the rate of moisture gain in the

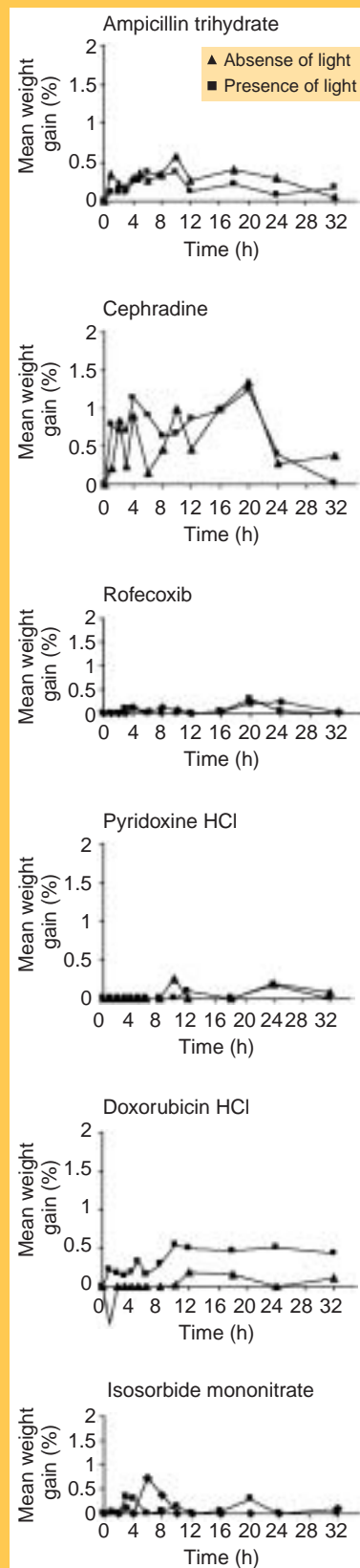


Figure 2: Moisture gain behavior of nonhygroscopic drug substances in the absence and the presence of light.

presence of light occurs in the case of benzyl penicillin sodium. Figure 3 shows that variable sensitivity also exists for excipients, although not to the same extent as for the drug substances.

No relationship was seen between inherent hygroscopicity and the influence of light. Drugs with less overall moisture gain in the dark (~40%) such as benzyl penicillin sodium show a greater influence of light, whereas sodium valproate, with a total moisture gain as high as 70%, is influenced to a much lesser extent. However, excipients show a typical pattern. As seen in Figure 3, most excipients gain as much as 5–25% RH in the dark, but none of the excipients show moisture gain at the levels seen in drugs such as ranitidine hydrochloride, sodium valproate, carbenicillin sodium, or benzyl penicillin sodium. This means that excipients are less likely than the drugs to gain moisture on exposure to light.

Conclusion

The phenomenon of acceleration of the rate of gain of moisture by light, which we first reported in previous studies (1,2), is found in this study to be a general occurrence, applicable to various hygroscopic drug substances and excipients. Therefore, this study suggests that formulation and packaging development, including stability testing protocol, for products containing hygroscopic drugs and excipients should include the study of the rate of moisture gain in the absence and the presence of light. This is particularly important for products that will be distributed in tropical countries, which not only have hot and humid environments, but also intense light.

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References

1. S. Singh et al., "Behavior of Uptake of Moisture by Drugs and Excipients under Accelerated Conditions of Temperature and Humidity in

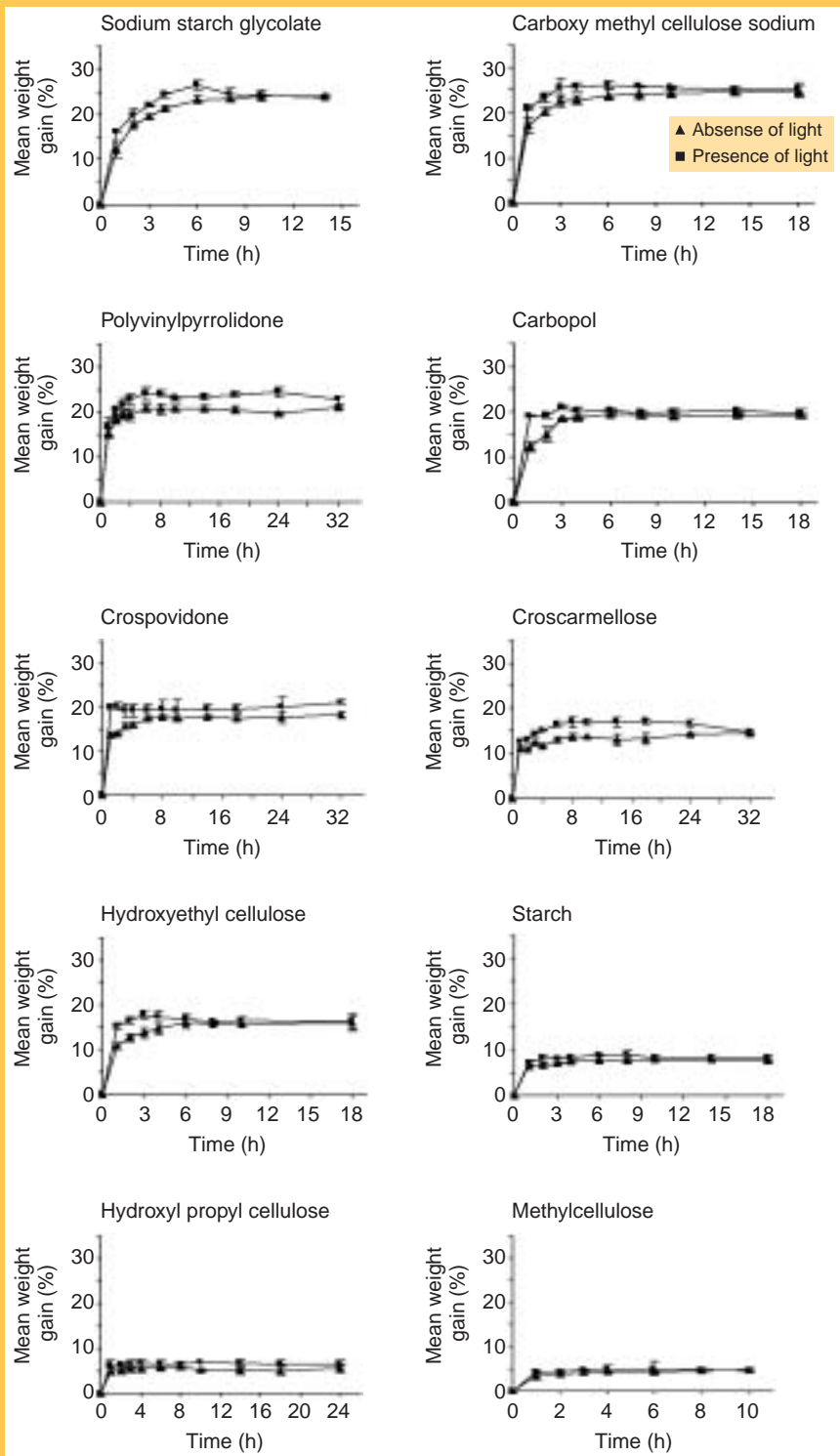


Figure 3: Moisture gain behavior of known hygroscopic excipients in the absence and the presence of light.

- the Absence and the Presence of Light. 1. Pure Antituberculosis Drugs and Their Combinations," *Int. J. Pharm.* **245**, 37–44 (2002).
2. H. Bhutani, T.T. Mariappan, and S. Singh, "Behavior of Uptake of Moisture by Drugs and Excipients under Accelerated Conditions of Temperature and Humidity in the Absence and the Presence of Light, Part II: Packaged and Unpackaged Unpackaged Antituberculosis Products," *Pharm. Technol.* **27**, 44–48 (2003). **PT**