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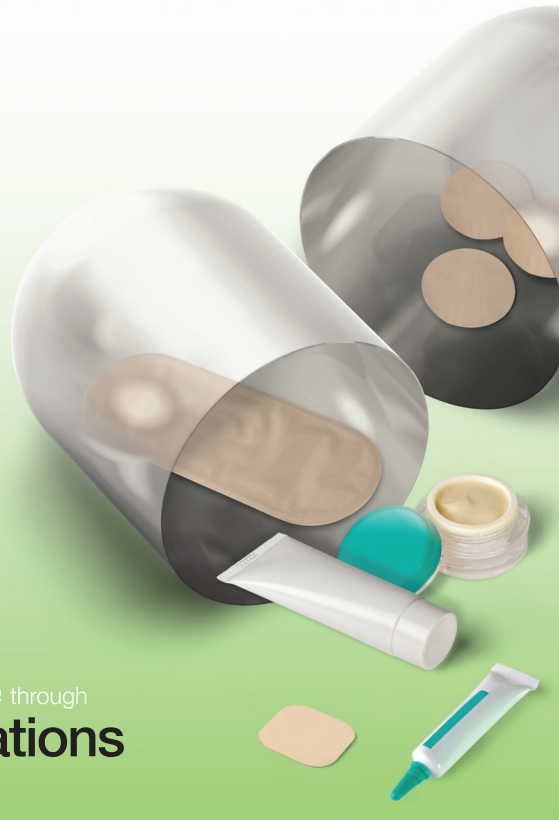
Healthcare
Solutions

Silicone Acrylate Hybrid Pressure Sensitive Adhesive

A Flexible System With Superior Compatibility for Transdermal Drug Delivery

Purpose

Common classes of pressure sensitive adhesives (PSAs) used in Transdermal Drug Delivery Systems (TDDSs) include silicone, acrylic and synthetic rubber. Historically, polymer blends utilized in the processing and manufacturing of TDDSs contained one or more classes of PSA. Blends of PSA have been shown to provide better wear adhesion and drug permeation properties [1]. A silicone acrylate (SilAc) hybrid PSA has been developed combining the advantages of silicone PSAs with that of organic PSA materials. The goal of this study was to determine the advantage of the SilAc hybrid system over blends of the neat PSA systems in terms of physical stability. Further, the flexibility of the SilAc hybrid PSA to modulate drug delivery profiles with varying silicone to acrylate ratios was evaluated.



Advancing healthcare through material innovations

Compatibility Study – Method

Placebo PSA/Excipients Blends (Figures 1A-1D)

- Wet placebo blends of silicone, acrylic and SilAc adhesives
- Physical blends: silicone to acrylic ratios 0/100, 25/75, 50/50, 75/25, 90/10, 100/0
- SilAc Hybrid PSAs: silicone to acrylic ratios 50/50, 75/25, 90/10
- Blendbacks (BB) from the 50/50 SilAc hybrid: final ratios 25/75, 75/25, 90/10
- To all blends above were added mineral oil (MO), dipropylene glycol (DPG) and oleic acid at 7.5% each, based on dry weight of the PSA, against control of neat PSAs

Blends with Ketoprofen (Figure 2) and Estradiol (Figure 3)

- Physical blends of silicone and acrylic adhesives with ratios 25/75, 50/50, 75/25
- SilAc hybrid adhesive with ratio 50/50 and 75/25
- Blendbacks (BB) from 50/50 SilAc hybrid: final ratio 25/75, 75/25
- Ketoprofen study: 10% ketoprofen drug and 10% oleic acid.
- Estradiol case: 1.5% estradiol, 6% oleyl alcohol, 9% dipropylene glycol, 7.5% Kollidon® VA 64

Compatibility Study – Results

- The physical blends of silicone and acrylic PSA showed phase separation, i.e. non-compatibility at all mixing ratios.
- SilAc hybrid PSA and backblends made thereof did not phase separate over the period of observation.
- Similar observations were made with dried films on microscopic slides and with neat PSA blends without excipients/drugs (not shown).

Figure 1A: Neat PSA blends

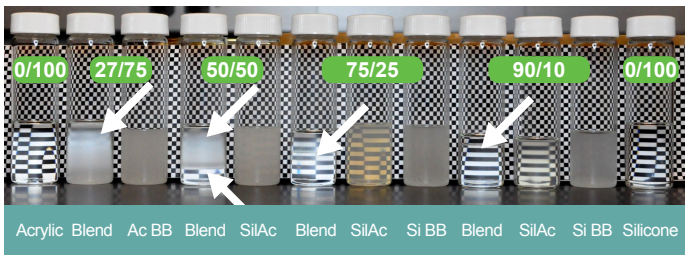


Figure 1B: PSA/mineral oil blends

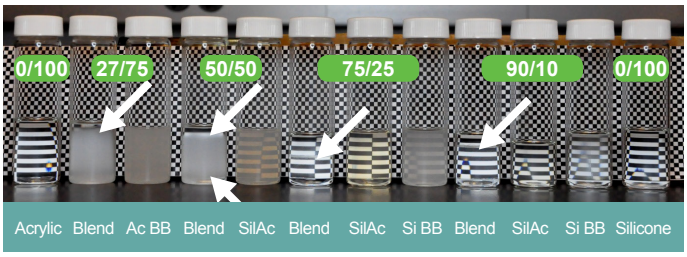


Figure 1C: PSA/dipropylene glycol blends

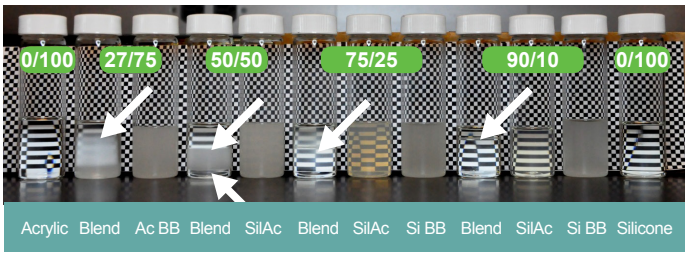


Figure 1D: PSA/oleic acid blends

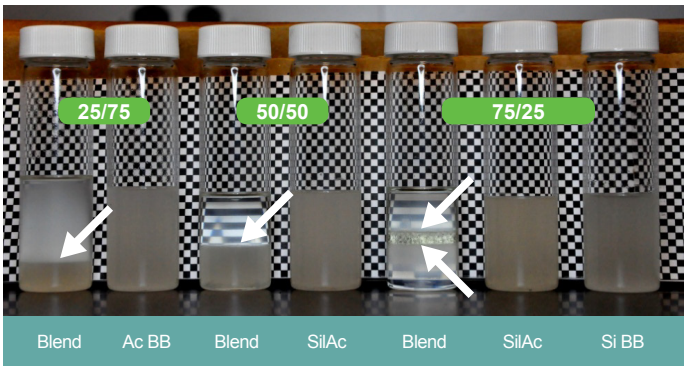


Figure 2: Ketoprofen wet blends

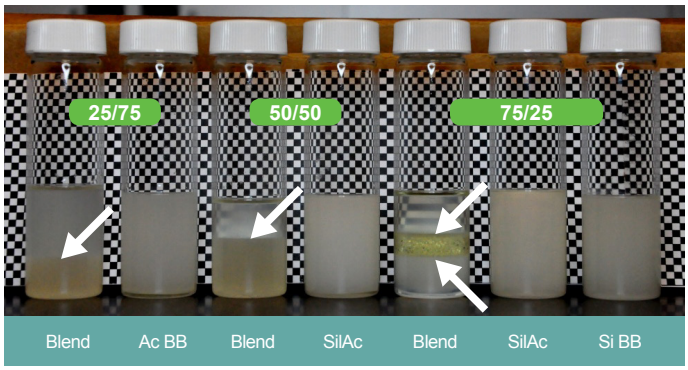


Figure 3: Estradiol wet blends

All placebo and drug blends were prepared by weighing the appropriate PSA(s) into glass vials, adding the appropriate amount of excipient and drug, and post-adding ethyl acetate as a process solvent to achieve a final percent solids solution of approximately 47.5%. The blends were mixed on a process rotator at 7 rpm for a minimum of six hours before any observations were made. Results illustrated here refer to observations after one month.

Skin Permeation Study – Method

Patch Preparation

- Selected blends with drug were casted on Scotchpak™ 9744 release liner. The laminates were dried for five minutes at RT, followed by five minutes at 92°C in a convection oven.
- The dried active matrix was laminated to Scotchpak™ 8038 backing.
- Coat weight: approximately 10.0 ± 0.5 mg/cm^2 (estradiol) and 11.0 ± 1.0 mg/cm^2 (ketoprofen)

Tested PSA Blends:

A) SilAc I Hybrid PSA with silicone-to-acrylic ratio of 50/50, 75/25 and 90/10, and SilAc II Hybrid PSA 50/50 (lower loading of high Tg acrylic monomer)

B) Physical blends of silicone and acrylic PSA at ratios of 75/25 and 25/75 and blendbacks from SilAc hybrid PSA 50/50, final silicone-to-acrylic ratios 75/25 and 25/75

Drug permeation was measured on a Logan Automated Franz Diffusion Cell using heat separated epidermis from human cadaver skin [National Disease Research Interchange (NDRI), with support from NIH grant 5 U42 RR00604]. The cell temperature was maintained at 32°C with magnetic agitation, and the receptor fluid was phosphate buffered saline (PBS). Samples of the solution were periodically taken and the drug concentrations in PBS were determined by UPLC. The ketoprofen study was run over 72 hours and no commercial TDDS was available as control. The estradiol permeation study was run over 84 hours and was fluxed against the Vivelle-Dot® (estradiol transdermal system) manufactured by Noven Pharmaceuticals, Inc. The estradiol control TDDS states a label claim of 0.156 mg/cm^2 drug concentration. All formulations were tested in triplicates.

Skin Permeation Study – Results

A) Varying silicone to acrylate ratios

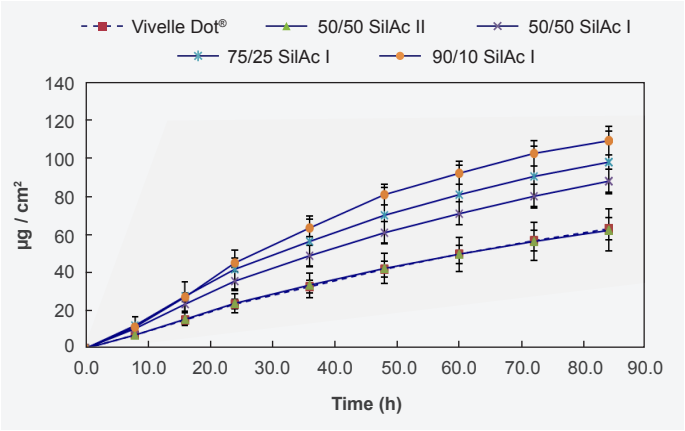


Figure 4: Estradiol

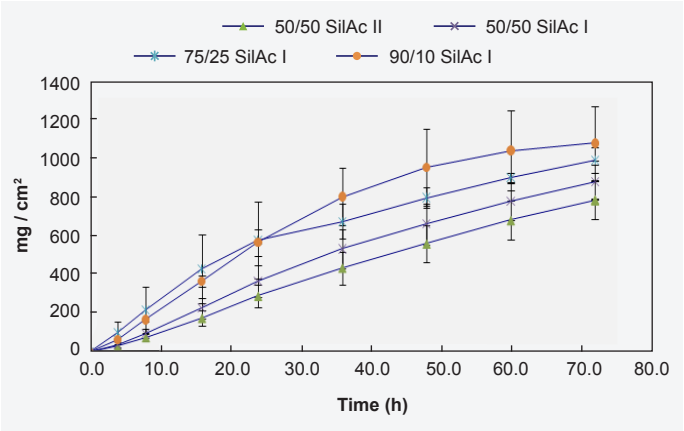


Figure 5: Ketoprofen

B) SilAc hybrid PSA versus physical blend

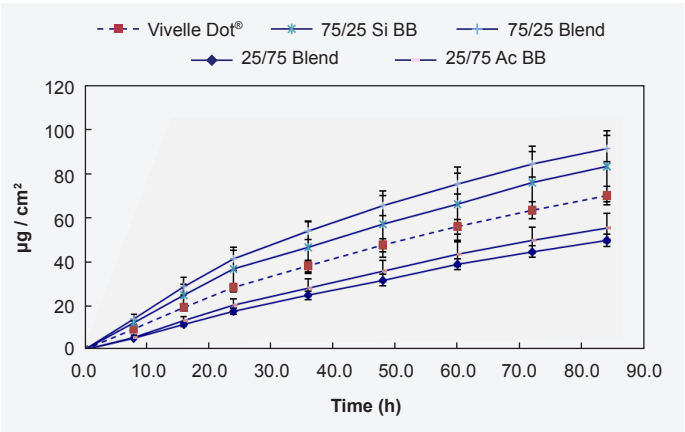


Figure 6: Estradiol

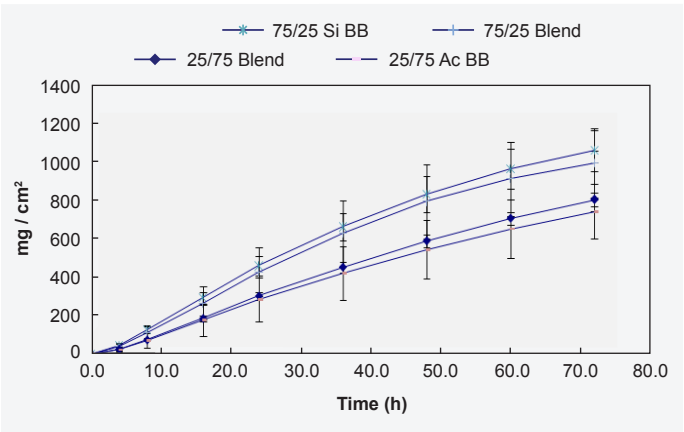


Figure 7: Ketoprofen

- The amount of drug permeated rose with increasing silicone-to-acrylic ratio. Type I and type II SilAc PSA have different release rates, SilAc II being significantly lower.
- Equivalent release rates were obtained from physical blends of silicone and acrylic PSA and from backblends of SilAc hybrid PSA with the corresponding final silicone-to-acrylic ratio.

Conclusion

- SilAc hybrid PSAs show improved compatibility versus physical blends of silicone and acrylic PSA materials.
- Starting from 50/50 SilAc hybrid, customized silicone to acrylate ratios can be obtained by blending back with silicone or acrylate adhesive. These backblends maintain the improved compatibility profile of SilAc hybrid PSAs.
- Drug flux profiles can be modulated with varying silicone to acrylic ratios. The flux results from hybrid material are equivalent to that of physical blends.
- Different acrylic monomer ratios in SilAc hybrid PSA result in different flux profiles. Therefore, the choice of acrylic monomer in the adhesives impacts the final drug delivery profile.
- SilAc hybrid PSAs are a novel, flexible silicone adhesive system combining the advantages of pure silicone and acrylic PSA materials and reaching superior physical stability.

References

[1] Woodard J. and Metevia V.; Transdermal Drug Delivery Devices with Amine-Resistant Silicone Adhesives: US Patent 4,655,767

- Loubert, G.; Mitchell, T. P. and Thomas, X; A Silicone Acrylate Hybrid Composition and Method of Making Same; Patent WO 2007/145996 A2
- Miranda J. and Sablotsky S.; Solubility Parameter Based Drug Delivery System and Method for Altering Drug Saturation Concentration: US Patent 5,474,783

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