J. Pharm. Pharmacol. 1985, 37: 722–725
Communicated April 12, 1985

COMMUNICATIONS

The use of strain gauges for radial stress measurement during tableting

P. D. Huckle*, M. P. Summers, *The School of Pharmacy, University of London, 29–39 Brunswick Square, London WC1N 1AX, UK*

The influence of size, configuration and positioning of die wall strain gauges on the measurement of radially transmitted stress developed during tableting was investigated. Calibration of strain gauges attached to a cutaway die wall was achieved by compression of rubber-like materials in the die, Breon Polyblend 504 being more effective than red rubber for this purpose. Hysteresis of response observed when calibrating a thin-walled die was possibly due to excessive distortion of the weakened die wall although the extent of this hysteresis varied with calibration material. The use of full bridge arrangements produced an increase in response when the compression site was moved away from the gauges. The opposite effect was seen when half bridge arrangements, using two active gauges, were used. The paradoxical effect observed when full bridge arrangements were used was shown to be due to straining of the compensating gauges. The dependence of die wall response on compact position was substantially reduced by the use of multiple gauges mounted along the die length and connected together to form a single gauge on each side of the die.

Measurement of the radially transmitted stress developed during uni-axial compaction of pharmaceutical powders was first proposed by Nelson (1955). The use of die wall stress measurements has included characterization of material properties (Ridgway et al 1969; Summers et al 1976), elucidation of bonding mechanisms (Carstensen & Toure 1980), and prediction of tablet capping tendency (Obiorah & Shotton 1976). Although workers have experimented with split dies (Long 1960), pins in the die wall acting on load transducers (Nelson 1955; Obiorah 1974), and photoelastic techniques (Ridgway 1966) to measure radial stress, strain gauges bonded into cutaways in the outer die wall still provide the most convenient method for such measurements.

Calibration of die wall strain gauges by compression of rubber-like materials within the die bore was suggested by Windheuser et al (1963). As a consequence of the apparent hydraulic behaviour of rubber, the pressure transmitted directly to the die wall can be assumed to be the same as that applied by the upper punch. Leigh et al (1967) calibrated strain gauges by forcing water under pressure into the die held between two plates. Subsequent calibration of the die using a rubber plug produced a die wall response of the same order, thus confirming this assumption. Further investigation into the calibration procedure was reported by Holzer & Sjogren (1979) who demonstrated that the position of the lower punch had a marked influence on the die wall response. Hysteresis of response was noted, the extent of which varied with calibration material. We now report the influence of calibration material, strain gauge size, configuration and position on the die wall signal.

Materials and methods

An instrumented Manesty E2 tablet press was used. The original lower punch and holder assembly were removed and replaced by a fixed lower punch arrangement (Ho et al 1979) which allowed bridging of the overload mechanism. Lower punch penetration into the die bore was adjusted by the insertion of hardened steel spacers under this assembly. The upper punch and lower punch assembly had strain gauges attached to facilitate monitoring of the applied and axially transmitted stresses, respectively. The armature of a displacement transducer mounted on the lower punch assembly was passed through an aperture in the die table to contact the upper punch holder, allowing measurement of the inter-punch face distance.

Two cutaway dies, each of 12 mm bore (Fig. 1) had strain gauges attached. Die A was cut away to leave a die wall thickness of 3 mm. 90° T-rosette gauges (Micromeasurements EA-06-125TA-120, Welwyn Strain Measurements, Basingstoke) were mounted in the cutaways midway along the die bore. The gauge connecting leads were joined at some distance from the die allowing reconnection into full or half bridge configurations. A wall thickness of 3 mm was also employed in die B but two larger gauges (Micromeasurements EA-06-250AE-350, Welwyn Strain

* Correspondence.

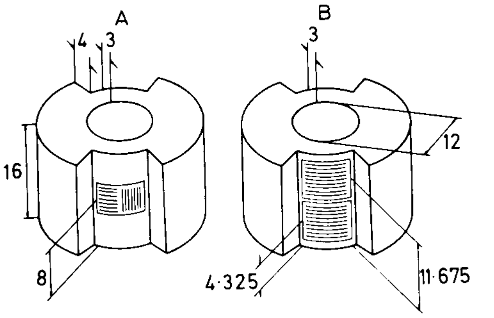


FIG. 1. Diagram of cutaway dies showing die wall thicknesses and strain gauge positions (all dimensions in mm).

Measurements, Basingstoke) were mounted horizontally in each of the cutaways.

The outputs from the displacement transducer and strain gauge bridges were conditioned by amplifiers and fed to a multichannel analogue-to-digital converter (Ortholog, Middlesex). Digitized signals produced by this instrument were read into a microcomputer.

Calibration of the die wall strain gauges was effected by compression of a plug of rubber-like material within the die. Spacers of 12 mm diameter and 4 mm thickness were produced from Breon Polyblend 504 (B.P. Chemicals, London) and red rubber (Gallenkamp, London) for this purpose. The press was operated manually and the applied axial stress and die wall signal were recorded simultaneously during both loading and unloading. This calibration procedure was repeated at various lower punch settings.

Results and discussion

Calibration material. The use of all four gauges on die A in a full bridge configuration revealed hysteresis of response when red rubber was used as the calibration material. The hysteresis was still observed, although the extent was reduced, when the calibration was repeated using Breon Polyblend 504 (Fig. 2). In both cases the hysteresis was maximal when the lower punch setting resulted in the plug being compressed close to the strain gauge centres. The hysteresis became less evident as the site of compression was moved up the die away from the gauges. It is proposed that this hysteresis of response may be partially due to excessive straining of the weakened die wall, although material effects also seem to play a contributory role. Breon Polyblend 504 was found to exhibit a more hydraulic response to applied axial stress than red rubber and was thus used as the sole calibration material in subsequent work.

Strain gauge configuration. A full bridge arrangement of the gauges on die A produced a minimal die wall response when the site of compression was located close to the gauges (Fig. 3). The response increased as the compression site was moved away from the gauges. A half bridge arrangement, using the two horizontally aligned gauges, produced a maximal response when the site of compression was located close to the gauges; the response decreased as the compression site was moved away from the gauges.

The die wall signal produced when the two vertically aligned temperature compensating gauges were used in a half bridge arrangement was also measured. Due to these gauges being located in the diagonally opposite arms of the bridge to the horizontally aligned gauges,

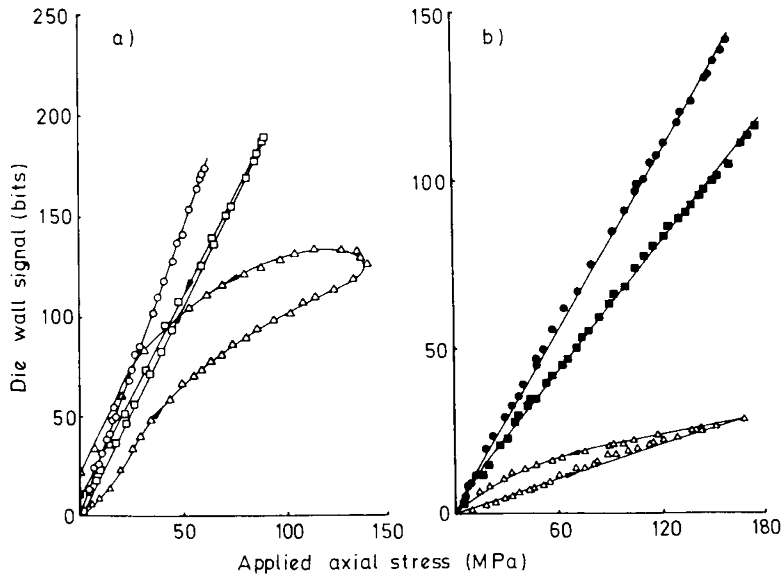


FIG. 2. The relation between die wall signal and applied axial stress for (a) red rubber (amplifier gain approx. 2000) and (b) Breon Polyblend 504 (amplifier gain approx. 500) at various lower punch settings. (Key: Distance from centre of strain gauges to centre of calibration spacer: △ = 1 mm, ■ = 3·7 mm, □ = 4 mm, ● = 5·7 mm, ○ = 6 mm.)

the signal produced was of opposite polarity. The signal was, however, maximal close to the gauges and decreased as the compression site was moved up the die, in agreement with the horizontal gauge signal. It is evident, therefore, that the vertically aligned gauges are not acting solely as temperature compensating arms of the bridge, but are strained about their active axis. The results for the various configurations of gauges on die A are shown in Fig. 3. The paradoxical effect observed when a full bridge configuration was used can be seen to be the result of summating the two half bridge signals. Compensating gauges attached to the die wall therefore affected the results because they were strained significantly, a finding unreported by previous workers (Summers et al 1976; Holzer & Sjogren 1979; Lipman 1982).

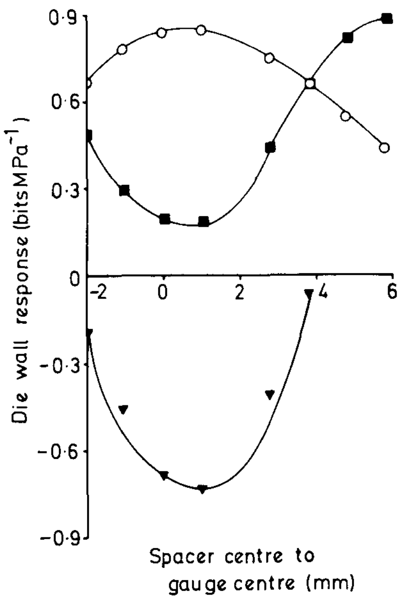


FIG. 3. The relation between die wall response and lower punch setting for strain gauge configurations on die A. (Key: ■ = full bridge configuration, ○ = horizontal gauges in half bridge configuration, ▼ = vertical gauges in half bridge configuration.)

Strain gauge size. Two larger horizontally aligned gauges were mounted in each cutaway of die B. The lower pair of gauges were connected in a half bridge configuration and the response to applied axial stress determined. The die wall signal was found to decrease as the site of compression was moved up the die, i.e. further from the gauges. When the upper pair of gauges were connected in a half bridge arrangement, the response was again found to increase as the compression site moved towards the gauges. In both cases, therefore, the maximal die wall response was obtained when compression occurred close to the gauges, the response decreasing as the compression site was located further from the gauges. The magnitude of the die wall response was influenced significantly by the lower punch setting in each case (Fig. 4).

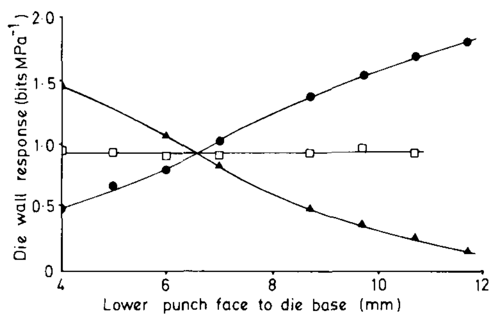


FIG. 4. The relation between die wall response and lower punch position for strain gauge configurations on die B. (Key: ● = upper gauges in half bridge configuration, ▲ = lower gauges in half bridge configuration, □ = combined upper and lower gauges in half bridge configuration.)

The upper and lower gauges on each side of the die were connected together to produce effectively two larger strain gauges. Each of these gauge components covered most of the cutaway area. The two sides were connected in a half bridge configuration and the die wall response measured at various lower punch settings. The influence of lower punch position on die wall response was found to be reduced significantly. The use of large gauges or multiple gauges connected together along the die length therefore allows the lower punch to be set at any level within the die whilst maintaining a constant die wall response to applied axial stress.

Conclusions

It is proposed that the hysteresis of response observed when a thin walled die was calibrated was due to excessive straining of the weakened wall. The choice of calibration material was, however, found to influence the extent of this hysteresis.

The die wall response increased as the compression site was moved away from the strain gauges when full bridge arrangements were used. This paradoxical effect was found to be due to the signal produced by the straining of the vertically aligned compensating gauges.

The use of vertically or horizontally aligned gauges alone in a half bridge arrangement produced more expected results where the die wall response was reduced as the compression site was moved away from the gauges.

The dependence of die wall response on compact position was found to be high in these half bridge configurations. The use of multiple gauges, adhered along the die length and connected together to form a single gauge component on each side of the die, substantially reduced this dependence on compact position.

REFERENCES

Carstensen, J. T., Toure, P. (1980) Powder Tech. 26: 199–204

Ho, A., Barker, J. F., Spence, J., Jones, T. M. (1979) J. Pharm. Pharmacol. 31: 471–472

Holzer, A. W., Sjogren, J. (1979) Int. J. Pharm. 3: 221–230

Leigh, S., Carless, J. E., Burt, B. W. (1967) J. Pharm. Sci. 56: 888–892

Lipman, E. C. (1982) Ph.D. Thesis Univ. of London

Long, W. M. (1960) Powder Metall. 6: 73–86

Nelson, E. (1955) J. Am. Pharm. Assoc. Sci. Edn. 44: 494–497

Obiorah, B. A. (1974) Ph.D. Thesis Univ. of London

Obiorah, B. A., Shotton, E. (1976) J. Pharm. Pharmacol. 28: 629–632

Ridgway, K. (1966) Ibid. 18: 176S–181S

Ridgway, K., Glasby, J., Rosser, P. (1969) Ibid. 21: 24S–29S

Summers, M. P., Enever, R. P., Carless, J. E. (1976) Ibid. 28: 89–99

Windheuser, J., Misra, J., Eriksen, S., Higuchi, T. (1963) J. Pharm. Sci. 52: 767–772

J. Pharm. Pharmacol. 1985, 37: 725–727
Communicated April 9, 1985

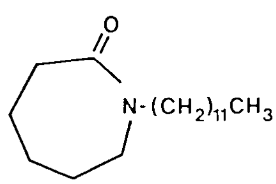
Facilitated transport of sodium salicylate across an artificial lipid membrane by Azone

JONATHAN HADGRAFT*, KENNETH A. WALTERS†, PAUL K. WOTTON, *Department of Pharmacy, University of Nottingham, University Park, Nottingham NG7 2RD, and †Fisons plc, Pharmaceutical Division, Loughborough, LE11 0RH, UK*

The ability of Azone (1-dodecylazacylcoheptan-2-one), a recently developed penetration enhancer, to facilitate the transport of sodium salicylate across an artificial lipid membrane has been investigated using the rotating diffusion cell, a well defined model for percutaneous absorption. Azone was found to be capable of enhancing the transport of the salicylate anion across an isopropyl myristate membrane, by using a pH gradient as the chemical driving force. The results indicate that Azone may be capable of forming ion pairs with anionic drugs.

Azone (I) is a comparatively new compound that has been shown to enhance the percutaneous penetration of many compounds (Stoughton & McClure 1983). Its exact mechanism of action is unknown. Previous work

(I)



in our laboratory has shown that long chain tertiary amines are capable of facilitating the transport of anionic drug molecules across artificial lipid membranes, by using a pH gradient to provide the driving force (Barker & Hadgraft 1981). The surface of the skin is reported to be slightly acidic, pH 4·2–5·6 and the lower layers are at the physiological pH of 7·4 (Katz & Poulsen 1971). We have therefore employed a pH gradient of 5–7·4 in our model system to represent the natural pH gradient that exists in skin.

The facilitated transport scheme, shown in Fig. 1, is established in the rotating diffusion cell. The epidermal barrier is simulated by a membrane filter impregnated with isopropyl myristate (IPM), a liquid representative of skin lipids (Poulsen et al 1968). In our previous experiments the carrier was incorporated into the IPM membrane. At the lower pH of the donor compartment/membrane interface the carrier protonates and can combine with the anions present to form ion pairs, in the interfacial region. The ion pairs can then partition into the bulk lipid phase and diffuse down their concentra-

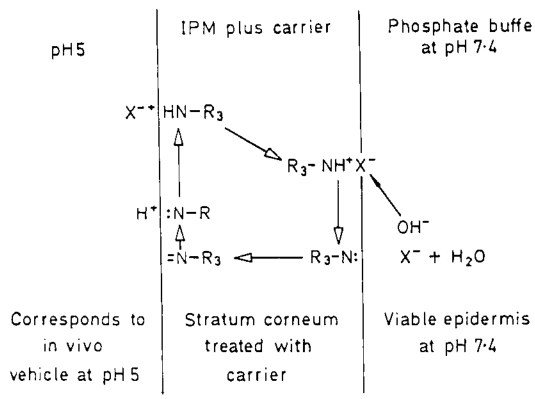


FIG. 1. Proposed facilitated transport scheme.

tion gradient to the opposite interface. In the interfacial region at the higher pH the carrier deprotonates to release the anions.

Azone has been reported to form the hydrobromide salt when treated with anhydrous hydrogen bromide (Stoughton & McClure 1983) and the same authors also suggest that Azone may be capable of forming salts with strong acids. Since Azone has a nitrogen atom in its ring structure which can be protonated it was therefore thought to be capable of operating within such a facilitated transfer scheme, although the pK_a of this

* Correspondence to: The Welsh School of Pharmacy, UWIST, PO Box 13, Cardiff, CF1 3XF, UK.