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Deceleration of light-induced changes of selected pharmacons by means of light screening films

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Abstract

Photo-induced changes in three pharmacons (Promethazine HCl, Carbidopa and Niphedipine), under exposure to light rich in UV component, could be characterised with the rate constants of the occurring processes. Partial rate constants could be determined after exposure to selected wavelength regions emitted by the light source. The most effective wavelength regions characteristic for the single pharmacons could be derived from the calculated partial rate constants. Six composite plastic films were applied for the desired light protection. A matrix LDPE film was particle filled — keeping the transparency of the extruded films — with colloidal titanium dioxide. By using three particle filled films of three different TiO_2 concentrations together with two commercial products, the photoactive ranges of wavelength could be cut off from the illuminating light. Satisfactory light stability of the pharmacons could be established with the help of the most appropriate single light screening films or with their best binary combination. © 1997 Elsevier Science S.A.

Keywords: Light sensitive pharmacons; Promethazine HCl; Carbidopa; Niphedipine; Light stabilisation; Light screening plastic film; High dispersity titanium dioxide

1. Introduction

Light-induced changes occur rather often in the production and storage of different goods. This phenomenon generated problems to be solved on the field of many industrial branches, including among others the textile and the pharmaceutical industries. The protection of coloured textiles belong to the actual tasks of the former branch, whereas the determination and control of photodegradation of pharmacons is a living problem of the second one [1]. Since, due to legal regulations, the addition of auxiliary products to the pharmacon is strictly prohibited, their protection against light-induced changes can mainly be solved by means of externally applied light screening systems [2]. It has been demonstrated [3] that ultrafine TiO_2 particle filled plastic films are very good UV absorbers providing this effect without toxic and migrating character and keeping the original transparency of the film unchanged. If the matrix of the film is light sensitive (e.g. polypropylene) this type of particle filling also provides simultaneously its light protection. Light sensitivity and its possible reduction has been the task of the present work related to three pharmacons: Promethazine HCl, Carbidopa and Niphedipine respectively. The light-induced changes in Niphedipine [2,4–10] and in Promethazine HCl [11,12] have already been studied, whereas that of Carbidopa has not yet been published. Local industrial experiences on their light sensitivity drew the attention to light stabilisation of these three pharmacons.

The aim of the work was the determination and reduction of light sensitivity of the three pharmacons mentioned. Isolation and characterisation of the products of light-induced changes, however, are not included. Experiments were carried out with pharmacon solutions, following the kinetics of their light-induced changes in the function of wavelength ranges emitted by the light source. Similar investigations were performed in systems, including appropriate light screening films between the light source and the pharmacon solution. The effect of the best light screening films was also tested on pharmacon pills.

2. Materials, equipment and testing methods

2.1. Materials

2.1.1. Pharmacons

The three pharmacons were placed at our disposal by EGIS Pharmaceuticals Ltd. (Hungary) and their structural for-

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mulae are set out together with their appropriate solvents in Table 1.

2.1.2. Light screening films

Tipolen® FB-243-54 (LDPE), (TVK Ltd., Hungary) was extruded to a matrix film and the same extrusion was performed with the blends of LDPE and TiO_2 pigments of three various concentrations. A further two commercial plastic films were also used (Table 2).

2.2. Equipment

A HP8482A (Hewlett Packard) diode array spectrophotometer was used for spectroscopic studies of pharmacon solutions and light screening films (LSF). ICS TEXICON TC4 (DATACOLOR) was used for reflective colour measurements. Brabender Plasti-Corder PL2000 (Brabender) was used for mixing and extrusion. The mixing die was of 350E type and that of the single screw extruder was 19/25D. The type of rotating disintegrator was RMA-1 (Rozmaring Ltd., Hungary). The device used for light exposure with the light intensity of 6 mW cm^{-2} is presented in Fig. 1.

2.3. Procedures

2.3.1. Master batch

10 g UV-TITAN® P160 previously mixed with 0.5 g Zn stearate was added to 100 g Tipolen® FB-243-54 (LDPE) and this was homogenised to a master batch on the Brabender Plasti-Corder PL2000, 350E mixing system. Working parameters: $t = 10$ min, $n = 20$ min^{-1}, $T = 180$°C.

2.3.2. Disintegration of the composite

The master batch was disintegrated by an RMA-1 disintegrator to a particle size of average 5 mm, applying rpm of 1440.

2.3.3. Extrusion

Films were extraded from granules on a Brabender Plasti-Corder single screw extruder. Working parameters: temperatures of zones, 170, 180, 190°C; temperature of die, 210°C; $n = 5$ min^{-1}; speed of conveyor belt, 6 m min^{-1}.

2.3.4. Exposure to light

Dissolved and solid pharmacons were exposed to light on the optical bench (Fig. 1) in such a way that the appropriate glass light screener (GLS) was placed between the light source and the substrate. Exposure lasted for up to 180 min.

3. Results and discussion

3.1. Light-induced changes of dissolved pharmacons

3.1.1. Kinetics of the reactions

Kinetics of light-induced changes of dissolved PH1, PH2 and PH3 was followed under exposure without screening and

Table 1
Pharmacons and solvents

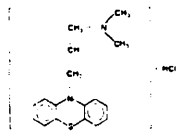
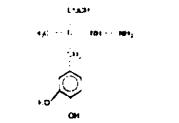
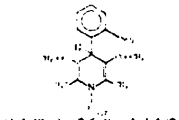
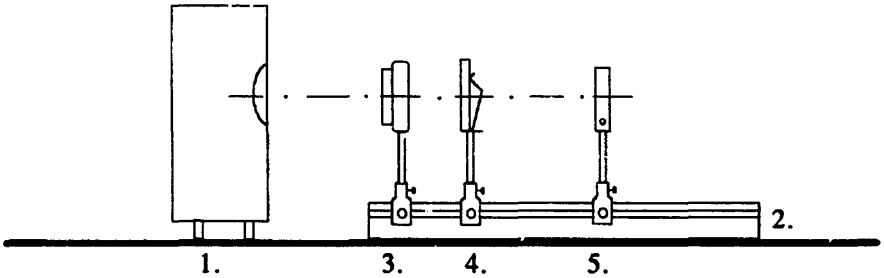
Name	Structure	Molar mass	Solvent	Concentration (mole l^{-1})
Promethazine HCl (PH1)	 10-[2-(dimethylamino)propyl]-phenothiazine monohydrochloride	320.9	bidistilled water	0.79×10^{-4}
Carbidopa (PH2)	 3-(3,4-dihydroxy-phenyl)-2-hydrazino-2-methyl-propionic acid)	226.23	bidistilled water	2.21×10^{-4}
Nipnedipine (PH3)	 (1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-piridin-3,5-dicarbonacid dimethylester)	346.3	ethyl alcohol	1.44×10^{-4}

Table 2
Light screening films

No.	Matrix polymer	Pigment g/100 g LDPE	Auxiliary 10 $^{-1}$g/100 g LDPE	Thickness of the film (μm)	$\lambda_{A(max)}$ [c] (nm)	A_{max} [f]
LSF1	Tipolen [a] FB 243-54	–	–	100	300	0.5
LSF1	Tipolen [b] FB 243-54	–	–	100	300	0.5
LSF2	Tipolen [b] FB 243-54	0.10 UV-TITAN [a] P160 [a]	5.0 Zn stearate [b]	100	300	1.5
LSF3	Tipolen [b] FB 243-54	0.15 UV-TITAN [a] P160 [a]	7.5 Zn stearate [b]	100	300	2.5
LSF4	Tipolen [b] FB 243-54	0.20 UV-TITAN [a] P160 [a]	10.0 Zn stearate [b]	100	300	4.0
LSF5 [c]	ONGROFOL [g]			250	248	4.0
	KTE101/361 PVC film, red	–	–		432	2.1
LSF6 [d]	RE35BRARL [g] polyethylene–therephtalate based multilayer film	–	–	100	–	transmittance in the UV range < 1% [g]

[a] UV-TITAN [a] P160, Kemira, Finland; average particle size, 20 nm.
[b] Zn Stearate, Merck, Germany.
[c] Ongropack Ltd, Hungary.
[d] 3M, USA.
[e] $\lambda_{A(max)}$, the wavelength at the absorption peak.
[f] A_{max}, the height of absorption peak.
[g] Disclosed by the producer.



1. 250 W high pressure mercury vapour lamp, 2. Standard triangular optical bench, 3. Quartz blend 4. Filter cell, 5. Cuvette holder

Fig. 1. Schematic diagram of the device used for light exposure.

behind glass light screeners (GLS), respectively. Changes in the UV–Vis absorption spectra of the dissolved pharmacons caused by light exposure were followed in the function of time. Evaluation of the kinetics was based upon changes in absorbance of selected highest or lowest absorbancies at the corresponding wavelength regions $\lambda_{selected}$ (λ_1, λ_2), as shown in Figs. 2–4.

$\lambda_1 = 340$ nm in Fig. 2 corresponds to an increasing absorbance in the course of exposure specific to the generation of the light-induced product from the original compound. It has been indicated [11] that the main light-induced change in PH1 is oxidation, therefore the increasing peak has to correspond to the increasing concentration the modified product. $\lambda_2 = 300$ nm was a wavelength where absorbance occurred in the solution of the original, and the modified product also had to show absorbance at the same wavelength. At the wavelength of 310 nm the detected constant absorbance throughout the whole duration of exposure indicates that similar specific absorbance was characteristic at the wavelength of both the original and the modified products.

$\lambda_1 = 310$ nm in Fig. 3 is characteristic for the absorbance of the unknown modified product, whereas $\lambda_1 = 254$ nm is characteristic for both the original and the modified products.

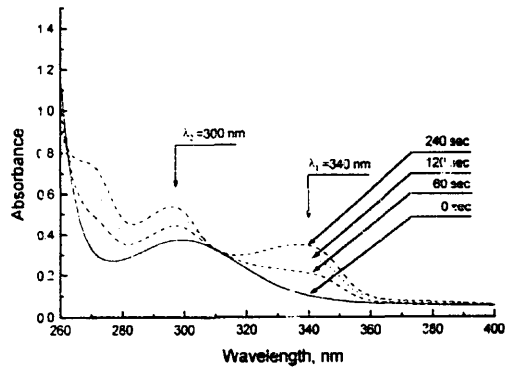


Fig. 2. Absorption spectra of Promethazine HCl (PH1) aqueous solution before and after irradiation to different times in the range of its UV spectrum from 260 to 400 nm.

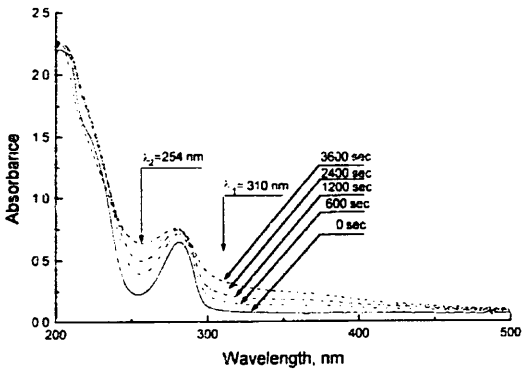


Fig. 3. Absorption spectra of Carbidopa (PH2) aqueous solution before and after irradiation to different times in the range of its UV–Vis spectrum from 200 to 500 nm.

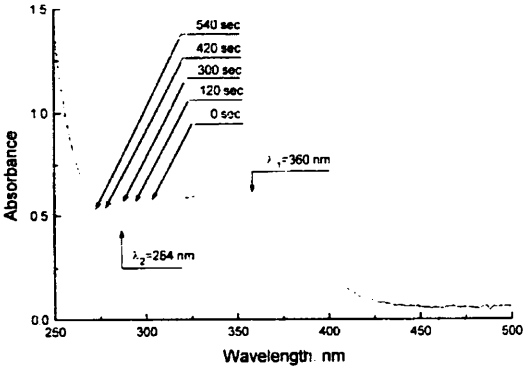


Fig. 4. Absorption spectra of dissolved Niphedipine (PH3) ethanol solution before and after irradiation to different times in the range of its UV–Vis spectrum from 250 to 500 nm.

but the increase in absorbance with the simultaneous increase of the concentration of the modified product is much more sensitive than that of the original one.

Note: Because of the extremely high light sensitivity of PH3 — in order to obtain proper data for evaluation — the intensity of the illuminating light had to be appropriately reduced in case of exposure to unscreened light. However, further experiments in screened systems have been carried out with the original light intensity.

$\lambda_1 = 360$ nm in Fig. 4 corresponds to the dihydro-pyridine structure [6] of the original PH3 molecule, whereas $\lambda_2 = 284$ nm is the absorption peak of the nitroso-derivative of PH3 [5]. The occurring isobestic point can be explained as a constant absorbance made up of the simultaneous decrease in the concentration of the original molecule and the generation of its modified derivatives at the same time.

It has been demonstrated [6] that the light-induced modification of PH3 is a first-order reaction. It has been assumed that a similar type of reaction is also relevant for light-induced changes of PH1 and PH2.

The calculation of rate constants was based upon Eq. (1).

$$k\tau = \ln\left(\frac{C_0}{C_\tau}\right) \tag{1}$$

where k is the reaction rate constant (s^{-1}), τ the time of exposure (s), C_0 the initial concentration of the pharmacon (mole l^{-1}), and C_τ the concentration of the pharmacon after τ s of exposure (mole l^{-1}).

As the absorption spectra of the light-induced modification of the pharmacons are unknown, it had to be assumed that A_τ might be the resultant absorbance of both the original and the modified pharmacon.

Consequently:

$$A_\tau = (1-p)A_0 + pA_p \tag{2}$$

where p is the degree of conversion from the original to the modified pharmacon ($0 \le p \le 1$), and A_p is the absorbance of the modified pharmacon after exposure of τ s.

Eq. (2) could be transformed to Eq. (3).

$$p = \frac{A_\tau - A_0}{A_p + A_0} \tag{3}$$

If $B = A_0 + A_\tau$ then

$$p = \frac{A_\tau - A_0}{B} \tag{4}$$

Eq. (5) can be derived from Eq. (1) and Eq. (4).

$$k = \frac{1}{\tau}\ln(1-p) \tag{5}$$

If the light-induced change of the pharmacon was a first-order reaction, a linear function must exist between $\ln(1-p)$ vs. τ. Appropriate values have to be found for B by means of iteration to fulfil this requirement. The two slopes ($k_{\lambda_1}, k_{\lambda_2}$), calculated at λ_1 and λ_2 wavelengths, should correspond to Eq. (6).

$$\frac{k_{\lambda_1} - K_{\lambda_2}}{k_{\lambda_2}} \le 0.1 \tag{6}$$

3.1.2. Light-induced changes reduced by GLS

As PH1 and PH2 are light sensitive only in the UV region, according to preliminary investigations, the respective glass light screeners GLS1, GLS3, GLS4, GLS5 and GLS6 were used in studies with them. PH3 is, however, light sensitive in the visible range too [5], therefore the glass light screeners GLS2, GLS4, GLS5, GLS6, GLS7, GLS8 and GLS9 were applied in the respective studies. The kinetics of the light-induced changes of pharmacons investigated are presented in Figs. 5–7.

Note: Because of the extremely high light sensitivity of PH3, the rate of its light-induced changes under unscreened light was very rapid, that is why the kinetic curve is missing from Fig. 7.

The rate constants can be calculated according to Eq. (7).

$$\sum_{\lambda} k_{\lambda_1-\lambda_2} + k_{\lambda_2-\lambda_3} + \ldots + k_{\lambda_i-\lambda_{i+1}} + \ldots + k_{\lambda_n-\lambda_{n+1}} \tag{7}$$

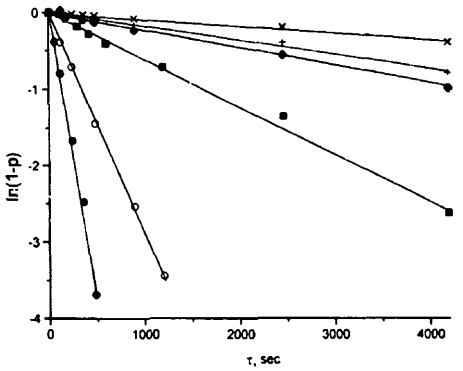


Fig. 5. Changes in kinetics of light induced modification of Promethazine HCl (PH1) caused by the quality of the used glass light screeners (see Table 3): ●, no screening; ○, GLS1; ■, GLS3; ◆, GLS4; +, GLS5; x, GLS6.

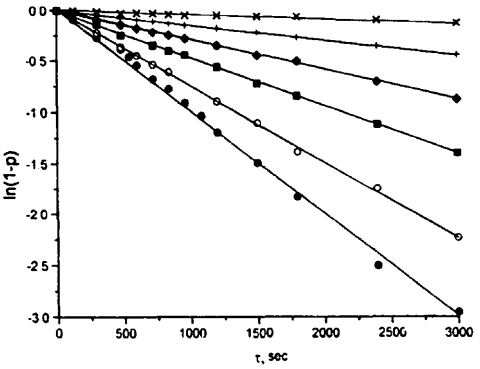


Fig. 6. Changes in kinetics of light-induced modification of Carbidopa (PH2) caused by the quality of the used glass light screeners (see Table 3): ●, no screening; ●, GLS1; ■, GLS3; ◆, GLS4; +, GLS5; x, GLS6.

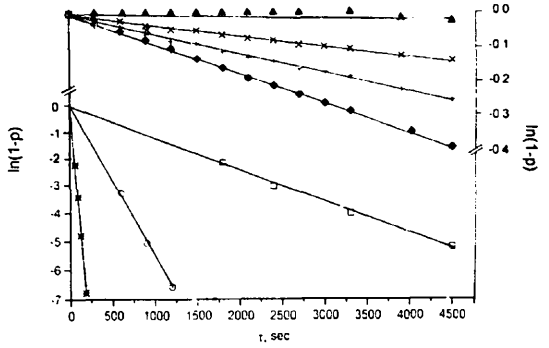


Fig. 7. Changes in kinetics of light-induced modification of Nipheclipine (PH3) caused by the quality of the used glass light screeners (see Table 3): *, GLS2; ○, GLS4; □, GLS5; ◆, GLS6; +, GLS7; x, GLS8; ▲, GLS9.

where λ_i is the shortest wavelength in the ith range (nm), λ_{i+1} the longest wavelength in the ith range (nm), $k_{\lambda_i-\lambda_{i+1}}$ is the reaction rate constant induced by the emitted light range from λ_i through λ_{i+1} (s^{-1}), and $\sum_\lambda k$ is the measured reaction rate constant enabling the calculation of the partial reaction rate constant (s^{-1}).

A factor that corrects the actual light intensity values of the light source at any wavelength range was introduced in Eq. (8).

$$f_{\lambda_i-\lambda_{i+1}} = \frac{\int_{\lambda_i}^{\lambda_{i+1}} P(\lambda)\,d\lambda}{\int_{\lambda_{min}}^{\lambda_{max}} P(\lambda)\,d\lambda} \quad (8)$$

where λ_{min} and λ_{max} are the shortest and the longest wavelengths in the spectrum of the light source and $P(\lambda)$ is the light intensity at wavelength λ (mW cm^{-2})

After dividing partial rate constants by the respective factor, a corrected value was obtained corresponding to the assumed chemical changes of the substrate, induced by exposure to light in the wavelength range between λ_i and λ_{i+1} but with the total light intensity of the light source emitted between λ_{min} and λ_{max}. The list of the corrected partial reaction rate constants is shown in Table 3.

The corrected rate constant values are plotted against the mathematical mean values of the respective wavelength ranges in Figs. 8–10.

The light-induced changes of PH1 occurred intensively under exposure below $\lambda = 300$ nm. An increase in the wavelength of incidental light decreased its sensitivity practically to zero around $\lambda = 400$ nm (see Fig. 8).

The light sensitivity of PH1 significantly exceeds that of PH2 at $\lambda = 420$ nm. The difference in rate constant disappears around $\lambda = 350$ nm. The rate constant of PH2 drops close to zero over $\lambda = 420$ nm.

Light sensitivity of PH3 exceeds by an order of magnitude that of PH1 in the wavelength region of 300 nm–420 nm.

Comparing the light sensitivity of the PHs in the visible range from 400 to 450 nm, the following can be concluded. At $\lambda = 400$ nm PH3 is three times more sensitive than the other two. At $\lambda = 420$ nm PH1 and PH2 are practically not sensitive to light, whereas the light sensitivity of PH3 is still well measurable. At $\lambda = 450$ nm none of the three pharmacons is light sensitive.

Evaluation of the data in Table 3 and in Figs. 8–10 suggested that elaboration of the most appropriate light screening films for particular wavelength ranges emitted by the light source, bringing about the fastest light-induced changes of the respective pharmacon, should be the next task of this work.

3.1.3. Composition of LSF for the improved light stability of pharmacons

For the desired screening of the light emitted by the light source, particle filled polymer films were foreseen. Consumer's demand was full transparency of the particle filled films without any turbidity. Consequently, ultrafine disperse pigments could only be applied [2]. TiO_2 pigment of average particle size 20 nm proved to be appropriate. To enable the uniform distribution of the particles in the matrix polymer, a

Table 3
List of the studied wavelength ranges, applied correction factors and calculated and corrected partial reaction rate constants of the pharmacons

$\lambda_i - \lambda_{i+1}$ (nm)	$f_{\lambda_i-\lambda_{i+1}} \times 10^{-3}$ (–)	Promethazine HCl (PH1) $k \times 10^{-3}$ (s^{-1})		Carbidopa (PH2) $k \times 10^{-3}$ (s^{-1})		Niphedipine (PH3) $k \times 10^{-3}$ (s^{-1})	
		Measured	Corrected	Measured	Corrected	Measured	Corrected
280–320	4.8	2.245	467.7	0.28	58.80	–	–
300–380	27.9	–	–	–	–	32.660	1170.63
320–380	13.3	0.365	27.44	0.71	53.40	–	–
380–400	3.8	0.039	10.25	0.14	38.72	4.346	155.78
400–430	36.1	0.093	1.79	0.10	2.03	1.065	20.60
430–480	4.2	–	–	–	–	0.030	7.11
480–530	6.3	–	–	–	–	0.030	4.07
530–600	13.6	–	–	–	–	0.000	0.00

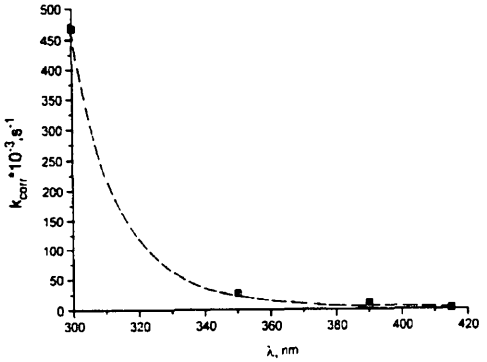


Fig. 8. Correlation between the corrected reaction rate constant and the respective mean wavelength values in the case of Promethazine HCl (PH1).

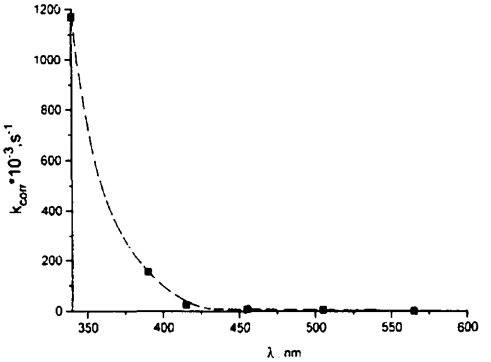


Fig. 10. Correlation between the corrected reaction rate constant and the respective mean wavelength values in the case of Niphedipine (PH3).

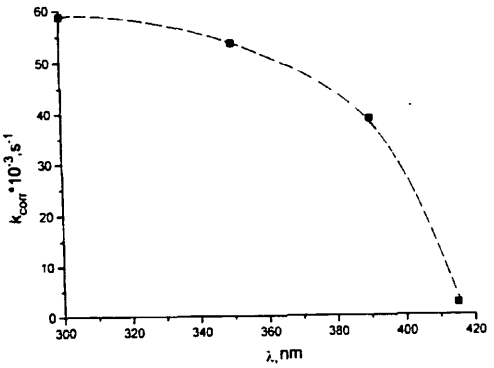


Fig. 9. Correlation between the corrected reaction rate constant and the respective mean wavelength values in the case of Carbidopa (PH2).

surfactant (Zn stearate) had to be added to the system. The compositions of the prepared films are shown in Table 2. These films can also be characterised by their UV–Vis spectra (Fig. 11).

For the selection of the most appropriate light screening film to a particular pharmacon, the following has to be considered: the light screening film, which exhibits the maximum absorbance (minimum transmittance) in the same wavelength range at which the particular pharmacon shows the highest reaction rate constant, can most effectively protect the pharmacon against light-induced changes (k_{corr} in Table 4). Pharmacons PH1 and PH2 LSF4 promised to be the most appropriate, although LSF2, 3, 6 have also been taken into consideration. No single light screening film seems to be appropriate for the protection of PH3. Only the simultaneous application of a binary system composed of LSF4 and 5 or LSF5 and 6 can solve the problem.

Light-induced modification of PH1 in the absence of light screening films was very fast. In the presence of the matrix polymer LSF1 no marked protection occurred. In the presence of LSF2 the protection was practically complete, and therefore the use of LSF3 and 4 with higher TiO_2 content was not necessary. The light protecting effect of LSF6 was nearly equal to that of LSF2 (Fig. 12).

The light-induced modification of PH1 was, in the absence of light screening films, significantly faster than that of PH2. The chemical change of PH2 was markedly slower in the presence of LSF1 although the rate of reaction of PH2 in this system was still higher then the respective rate of PH2 without any light screening film. The light screening effect of TiO_2 filled films was significant and the protection grew up to 0.15% particle containing LSF3 but no further improvement was caused by LSF4. Light protecting effect of LSF6 was

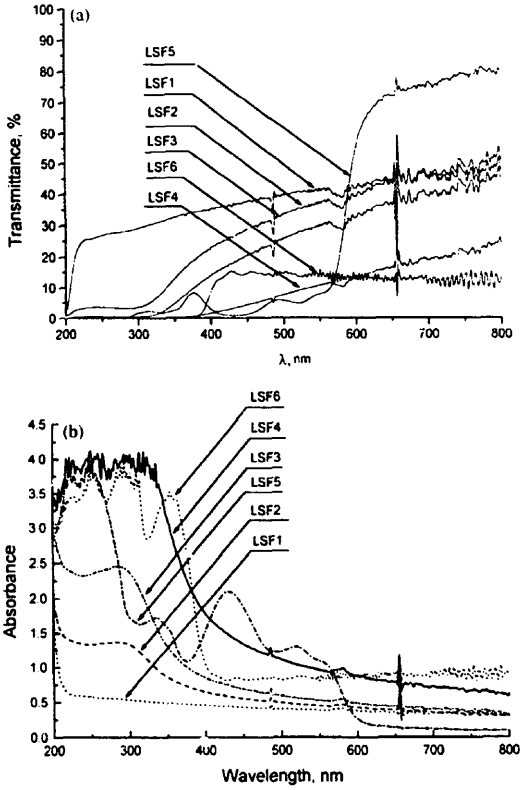


Fig. 11. UV–Vis spectra of light screening films disclosed in Table 2. (a) λ vs. transmittance, (b) λ vs. absorbance.

Table 4
Glass light screeners

No.	λ_c (nm)	Transmittance (%)	
		In the screened region ($\lambda > \lambda_c$)	In the transmitted region ($\lambda < \lambda_c$)
GLS1	280	< 0.5	> 97.5
GLS2	300	< 0.6	> 98.7
GLS3	320	< 0.5	> 98.3
GLS4	380	< 0.7	> 99.2
GLS5	400	< 0.9	> 96.2
GLS6	430	< 1.1	> 96.4
GLS7	480	< 1.8	> 97.8
GLS8	530	< 2.9	> 98.5
GLS9	600	< 3.0	> 95.5

λ_c, upper limit of the cut off wavelength region.

higher than that of LSF2 but lower than that of LSF3 (see Fig. 13).

The light-induced change of PH3 was the fastest in the absence of light screening films among the three pharmacons studied. In the presence of LSF1, 2, 3, 4, 5 and 6 the rate of the light-induced change of PH3 decreased, but the reduction was not sufficient. Since PH3 is sensitive both in the UV and Vis regions, best protection could be expected only from the

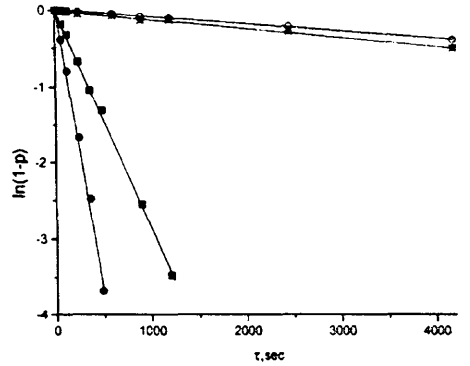


Fig. 12. Light-induced change of Promethazine HCl (PH1) in the presence of light screening films: ●, no screening; ■, LSF1; *, LSF2; ○, LSF6.

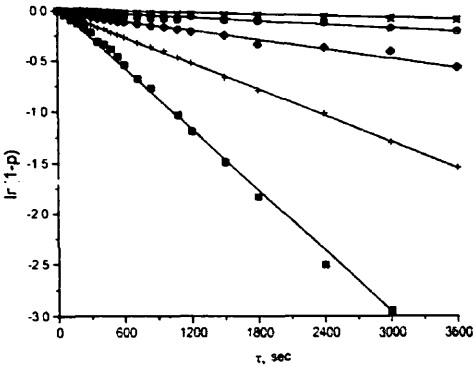


Fig. 13. Light-induced change of Carbidopa (PH2) in the presence of light screening films: ■, no screening; +, LSF1; ◆, LSF2; ●, LSF6; *, LSF3.

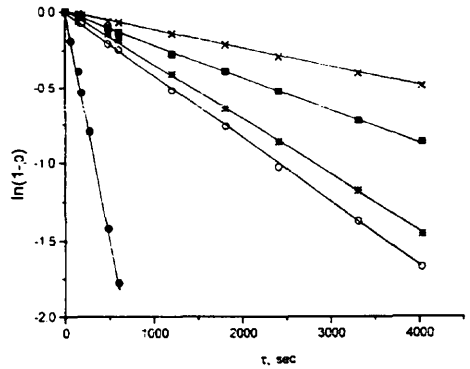


Fig. 14. Light-induced change of Niphedipine (PH3) in the presence of light screening films: ●, no screening ($I_{\lambda,\tau} = 0.5$ mW cm^{-2}); *, LSF3; ■, LSF5; x, LSF4 + LSF5; ●, LSF6.

combination of LSF4 and 5. Experimentally it could be verified that this combination (i.e. the two films behind each other and between the light source and the dissolved PH3) slowed down most significantly the studied light-induced reaction of PH3 (Fig. 14).

New reaction rate constants related to the selected combinations of pharmacon–LSF systems could be calculated and are presented in Table 5.

Table 5
Changes in the reaction rate constant of the pharmacons measured behind the selected light screening films

Films	Pharmacons								
	Promethazine HCl (PH1)			Carbidopa (PH2)			Niphedipine [a] (PH3)		
	k_0	k_i	k_i/k_0	k_0	k_i	k_i/k_0	k_0	k_i	k_i/k_0
	$\times 10^{-4}$		$\times 10^{-2}$	$\times 10^{-4}$		$\times 10^{-2}$	$\times 10^{-4}$		$\times 10^{-2}$
LSF2	76.9	0.9	1.1	–	–		–	–	–
LSF3	–	–	–	9.8	0.2	2.3	29.6	33.5	12.0
LSF3 + LSF5	–	–	–	–	–	–	29.6	1.2	4.0

k_0, measured rate constant without LSF; k_i, measured rate constant behind LSFi (i = serial number of LSF).
[a] Due to high light sensitivity of PH3, its k_0 value determined at 0.5 mW cm^{-2} illumination intensity instead of the usually used 6 mW cm^{-2} intensity.

Note: For the calculation of the rate constant in the case of unscreened PH3 the values obtained with reduced intensity of light source were applied.

3.2. Light-induced changes of pharmacons in pills

The most appropriate LSFs for the protection of dissolved pharmacons were investigated as protectors in the light-induced changes of the same pharmacons in pills. Experiments with PH3, however, could not be performed, because a strong change in the colour of the pill was observed already under the action of the light of the reflective colorimeter. The results of the investigations with the pills of the two further pharmacons (PH1 and PH2) are shown in Figs. 15 and 16.

It can be understood that the rather fast change in the colour occurs exclusively on the surface of the pill and the action of the light was negligible within it throughout the duration of light exposure. The change in colour of PH1 was rapid if no LSF had been used, ($\Delta E_{ab}^* = 11$ after 15 min). In case of LSF2, however, no detectable change in colour ($\Delta E_{ab}^* = 1$) occurred within the first 15 min of exposure. A remarkable change in colour ($\Delta E_{ab}^* = 11$) occurred — without light screening — within 15 min in the case of PH2, whereas exposure for 90 min was necessary under identical conditions for a similar marked change in the colour of PH1. In case of LSF3 the change in colour of PH1 was $\Delta E_{ab}^* = 1$ after 40 min and $\Delta E_{ab}^* = 2$ after 90 min of light exposure. It can be concluded that the same LSF provided the best protection against light-induced decomposition of a pharmacon regardless of its dissolved or solid state.

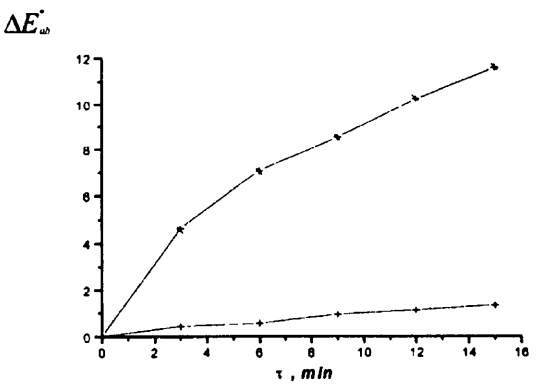


Fig. 15. The change in colour of Carbidopa (PH2) pills induced by light exposure: *, no screening; +, LSF2.

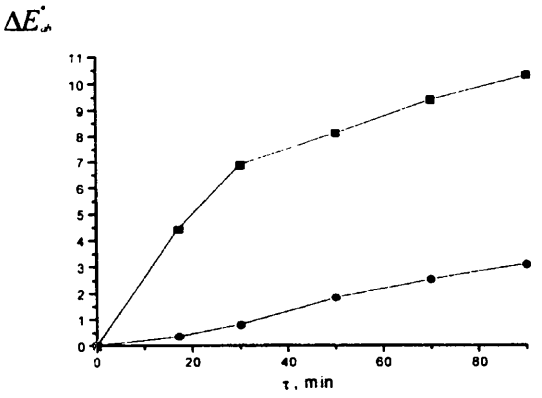


Fig. 16. The change in colour of Promethazine HCl (PH1) pills induced by light exposure: ■, no screening; ●, LSF3.

4. Conclusions

The photo-induced changes of the pharmacons PH1 and PH2 are induced by the UV radiation of the light source ranging from $\lambda = 200$ through 450 nm. One possible way to neutralise the action of the light in this case was the application of light screening films filled with identical sized particles (UV-TITAN® P160) but in different concentrations. The PH3 was light sensitive in the region of $\lambda = 200$–420 nm. Light stabilization of the latter pharmacon could be achieved by the simultaneous use of two LSFs, one of which was protective in the UV region and the other one in a visible range. No difference in sensitivity could be detected for a particular pharmacon between its dissolved state and its surface in solid state. The best light stabilisation was performed by LSF systems which had the highest absorbance at the same wavelengths where the pharmacon showed its highest partial rate constants.

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