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ORIGINAL ARTICLE

Rapid assay of the comparative degradation of acetaminophen in binary and ternary combinations

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Abstract The study is intended to monitor the comparative degradation rates of acetaminophen in binary and ternary combinations by UV–vis spectroscopy. The drugs were exposed to UV-rays in blister packing. The exposition time was 24, 48 and 72 h for both shorter and longer wavelengths. The problem of overlapping UV bands of aspirin and caffeine with acetaminophen was solved by extracting them in diethylether, therefore, we developed a straightforward, rapid and accurate assay method for measuring acetaminophen concentration in binary and ternary mixtures and to monitor its degradation.

1. Introduction

The quality and the stability of pharmaceutical drugs are of fundamental significance for patient's safety and rapid health recovery. Different environmental factors such as humidity, temperature and UV (ultraviolet) light influence the stability (Marin and Barbas, 2004) of these drugs, since these elements produce various degradants. In consequence, the presence of degradant metabolites profoundly influences the efficacy of these medicines. In some cases, the degraded products absolutely alter the pharmacology of a drug leading to serious side effects. For example, the primary degradation product of *Paracetamol* (or *Acetaminophen*) is *p*-aminophenol that is reported to have teratogenic effects (Prescott, 1996). *Paracetamol* or *N*-acetyl-*p*-aminophenol is the most widely used analgesic, antipyretic and anti-inflammatory drug. *Paracetamol* is often recommended and used in combinations (Daniels et al., 2011; Ortiz et al., 2011) with other analgesic drugs such as *Aspirin* and *Caffeine*. It is thus imperative to develop a method for simultaneous analysis (Okamoto et al., 2005) and

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quantification of these drugs. The simultaneous analysis in binary and ternary combinations is generally performed on RP-HPLC (Hadada et al., 2009), often assisted by gradient elution (McEvoy et al., 2007), which is a time-consuming and expensive method considering the needs of an advanced analytical instrument. In the present study, a simple, accurate, cost effective and relatively quick assay method is developed for the quantification of *Acetaminophen* (Viaene et al., 2002). To monitor the comparative degradation and stability of *Acetaminophen* in the aforementioned single, binary and ternary combinations that are named as *A*, *B* and *C* respectively, the drugs were subjected to forced degradation via UV-rays for 24, 48 and 72 h and the rapid assay was performed via UV–vis spectroscopy.

2. Experimental

All the analytical grade chemicals and reagents were purchased from Merck and used without further purification. *A*, *B* and *C* were gifted by the local pharmaceutical laboratory. The complete specification of all the drugs is described in Table 1.

The drugs were first exposed to UVGL-58 Handheld UV lamp at a shorter wavelength of 254 nm and at a longer wavelength of 365 nm. The exposition time for all the drugs was 24, 48 and 72 h, respectively. Since all these drugs also contain excipients, therefore, average-weight of 20 tablets equivalent to 100 mg of *Paracetamol* from each drug were dissolved in three 100 mL volumetric flasks separately taking methanol as the solvent. In the case of drugs ***B*** and ***C***, the methanolic solution was treated further with diethylether batch-wise so as to extract the *Caffeine* and *Aspirin* in ether, leaving behind *Paracetamol* in methanol. Subsequently, 1 mL of methanolic solution was diluted to 100 mL with 0.1 N NaOH and the assay was performed. All the measurements were performed on a UV–visible spectrophotometer, SHIMADZU UV-1700 pharma spectrophotometer, using UV *probe* software.

3. Results and discussion

In the UV–vis spectrum, *Paracetamol* exhibits maximum absorbance (λ_{max}) at 243 nm in methanol, while *Aspirin* and *Caffeine* have λ_{max} in proximity to 237 nm and 273 nm, respectively. As mentioned in Table 1, *Caffeine*, being in lower amounts in ***B*** and ***C***, partly interferes with the absorption band of *Paracetamol*. On the other hand, *Aspirin*, being in excess quantity and having λ_{max} close to that of *Paracetamol*, strongly overlaps in its absorption region. Thus, the interference is less evident in ***B*** but is noticeably higher in the case of ***C***, as shown in Fig. 1 (in gray). It is obvious that there exists a strong overlapping and it is difficult to identify a sharp absorption band of *Paracetamol*, which makes the quantification of *Paracetamol* a tedious task for quality control and degradation analysis.

Table 1 The drugs used in analysis with complete specification and formulation.

Drugs	Formulations
A	Paracetamol 500 mg
B	Paracetamol 500 mg + Caffeine 65 mg
C	Paracetamol 200 mg + Caffeine 30 mg + Aspirin 300 mg

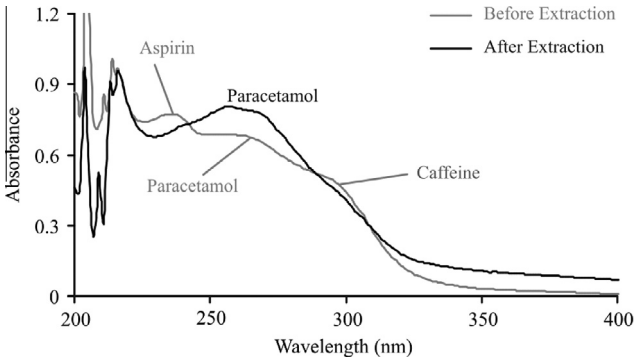

Figure 1 Scan of drug ***C*** before and after extraction which confirms that aspirin and caffeine have been removed.

This problem was solved by the solvent extraction process. *Aspirin* and *Caffeine* have reasonably good solubility in non-polar solvents such as diethylether, while *Paracetamol* is more soluble in methanol. Therefore, at first the methanolic solution of ***B*** and ***C*** was treated with diethyl ether in a batch-wise process. In this way, *Aspirin* and *Caffeine* were extracted into diethyl ether leaving behind *Paracetamol* in methanol. The UV-spectroscopic scan of the final dilution of methanolic *Paracetamol* in 0.1 N NaOH clearly demonstrates a sharper absorption band with λ_{max} equal to 256 nm i.e. free of any interference, as shown in Fig. 1 (in black). In 0.1 N NaOH, the absorbance is much higher in comparison to methanol and that is why the final dilutions were preferred in 0.1 N NaOH. The scans of standard *Paracetamol* solution in 0.1 N NaOH also exhibit the same λ_{max} value.

In the next step, all three types of tablets in packed blisters were exposed to UV-rays of shorter and longer wavelengths for a time period of 24, 48 and 72 h. The continuous exposure to UV-light leads to extensive degradation of *Paracetamol* including binary and ternary mixtures, albeit the decomposition trend and the percent degradants are different in single, binary and ternary combinations. The degradation results upon exposition to shorter and longer wavelengths are reported in Tables 2 and 3, respectively.

It is evident that at both the shorter and the longer wavelengths, the degradation rate is higher in ***B*** and ***C*** as compared to ***A***, which contains only one active ingredient. This could be attributed to the presence of *Caffeine* that, in some way, catalyzes the degradation of *Paracetamol* under UV-light. The presence of *Aspirin*, on the other hand, seems to have a little influence on the degradation of *Paracetamol* since the decomposition profiles of ***B*** and ***C*** are very much comparable. Furthermore, the degradation rate is higher at shorter wavelength, which may be ascribed to the higher energy associated with the 254 nm UV-rays.

After 72 h, nearly half of the active amount of *Paracetamol* is degraded inside original blister packing at shorter as well as longer wavelengths, which also indicates that the blister packaging is not resistive toward UV-light and thus could not ensure the environmental stability of these drugs over prolonged durations. The percentage error for all three drugs at all intervals in Table 2 and Table 3 were calculated. It was found that there was significant difference among all the drugs exposed for 24 and 48 h suggesting a certain degradation pattern at initial stages. However, there was no significant

Table 2 The degradation results of ***A***, ***B*** and ***C***, when exposed to UV-rays of a shorter wavelength i.e. 254 nm for different durations.

Drugs exposition time	***A***		***B***		***C***	
	Initial absorbance = 0.375		Initial absorbance = 0.394		Initial absorbance = 0.364	
	Absorbance	Degradation (%)	Absorbance	Degradation (%)	Absorbance	Degradation (%)
After 24 h	0.350	6.67	0.348	11.67	0.322	11.53
After 48 h	0.303	19.20	0.295	25.12	0.275	24.45
After 72 h	0.191	49.06	0.179	54.56	0.171	53.02

Table 3 The degradation results of ***A***, *B* and ***C***, when exposed to UV-rays of longer wavelength i.e. 365 nm for different durations.

Drugs exposition time	***A***		***B***		***C***	
	Initial absorbance = 0.375		Initial absorbance = 0.394		Initial absorbance = 0.364	
	Absorbance	Degradation (%)	Absorbance	Degradation (%)	Absorbance	Degradation (%)
After 24 h	0.363	3.20	0.373	5.32	0.349	4.12
After 48 h	0.318	15.20	0.317	19.54	0.302	17.03
After 72 h	0.199	46.93	0.181	54.06	0.173	52.47

difference, when they were exposed for 72 h both at shorter and longer wavelengths. This indicates that exposing a drug for a longer period of time leads to pronounced degradation of acetaminophen in all drugs despite high or low energy radiations.

4. Conclusion

In summary, a rapid assay methodology based on solvent extraction and fast UV-spectroscopic analysis is reported. In addition, this method is successfully employed to study the comparative degradation of *Paracetamol* (or *Acetaminophen*) in single, binary and ternary combinations. The solvent extraction with diethylether offers selective measurement of *Paracetamol* concentration, without the interference of other substances like *Caffeine* and *Aspirin*. The presence of *Caffeine* in binary and ternary drugs facilitates the degradation of *Paracetamol* under UV-light, which means that caffeine photo-catalyzes the decomposition process. In future, a detailed HPLC analysis of the exposed drugs and the structural characterization of the degradants would be combined with UV–vis spectroscopy to further validate these results and to obtain more expedient comprehension of the degradation mechanism and the precise role of *Caffeine* and *Aspirin* in UV-degradation of *Paracetamol*.

References

Daniels, S.E., Goulder, M.A., Aspley, S., Reader, S., 2011. Pain 152, 632.

Hadada, G.M., Emarab, S., Mahmouda, W.M.M., 2009. Talanta 79, 1360.

Marin, C., Barbas, J., 2004. Pharm. Biomed. Anal. 35, 1035.

McEvoy, E., Donegan, S., Power, J., Altria, K., 2007. J. Pharm. Biomed. Anal. 44, 137.

Okamoto, H., Nakajima, T., Ito, Y., Aketo, T., Shimada, K., Yamato, S., 2005. J. Pharm. Biomed. Anal. 37, 517.

Ortiz, M.I., Ponce-Monter, H.A., Mora-Rodriguez, J.A., Barragan-Ramirez, G., Barron-Guerrero, B.S., 2011. Eur. J. Obstet. Gynecol. Reprod. Biol. 157, 22.

Prescott, L.F., 1996. Paracetamol (Acetaminophen) A Critical Bibliographic Review. Taylor & Francis, London.

Viaene, E., Chanteux, H., Servais, H., Mingeot-Leclercq, Marie-Paule, Tulkens, P.M., 2002. Antimicrob. Agents Chemother. 46, 2327.