Anne-Claire Bonnaure*, Romain Bellay, Pauline Rault, Marie-Antoinette Lester and Pierre-Nicolas Boivin

Physicochemical Stability of 5 mg/mL Pediatric Prednisone Oral Suspension in Syrspend® SF PH4

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Abstract

Background: Prednisone is a corticosteroid used in several inflammatory diseases and cancers. In France, no available prednisone drinkable formulation exists. Instead, an oral syrup of prednisone with ethanol, sodium benzoate and simple syrup is produced. However, sodium benzoate can induce neonatal icterus and alcohol is not authorized for children below 3 years of age. The aim of this study was to determine the stability of 5 mg/mL prednisone oral suspension in a commercial compounding excipient: Syrspend® SF PH4.

Methods: Three batches of oral suspensions were prepared, using micronized prednisone and Syrspend® SF PH4. They were packaged in amber glass vials and stored at room temperature. On day 0, 1, 4, 10, 30, 60 and 90, we observed physical and chemical stability (pH measurement, osmolality measurement, residual concentrations of prednisone and degradation product identification). A stability indicating method was developed using high performance liquid chromatography with Ultraviolet detection at 254 nm.

Results: Prednisone concentrations remained stable within ± 5% of nominal values for 60 days. No degradation product and change of physicochemical properties were detected.

Conclusion: This study showed that 5 mg/mL prednisone oral suspension in Syrspend® SF PH4 is stable for 60 days, at room temperature and protected from light.

Keywords: suspension, formulation, excipient, stability, HPLC (Hight Perfomance/Pressure Liquid Chromatography), pediatric

***Corresponding author: Anne-Claire Bonnaure,** CHU de Rennes, 2 rue Henri Le Guilloux, 35000 Rennes, France, E-mail: anne-claire.bonnaure@hotmail.com

Romain Bellay, Pauline Rault, Marie-Antoinette Lester, Pierre-Nicolas Boivin, CHU de Rennes, 2 rue Henri Le Guilloux, 35000 Rennes, France, E-mail: romain.bellay@hotmail.fr; pauline.rlt@gmail.com; marie-antoinette.LESTER@chu-rennes.fr; pierre-nicolas.BOIVIN@chu-rennes.fr

Introduction

Prednisone (Figure 1) is a glucocorticosteroid usually used in several inflammatory pathologies and cancers. Low dose prednisone is used for anti-inflammatory activities, while high dose prednisone is employed for immunosuppressive purposes [1].

This drug is usually used in pediatric oncology and hematology units. To facilitate the pediatric use, drinkable formulations of prednisone are preferred over oral solid forms. However, no available prednisone drinkable formulation exists (no commercial syrup or ATU: Temporary Authorization for Use) in France and only tablets of prednisone are available [1].

Despite this, a few studies on liquid oral formulations have been reported [2, 3]. For several years, an oral syrup of prednisone with alcohol (ethanol), sodium benzoate, and simple syrup [4] was prepared in our hospital. The stability of this preparation was maintained for 56 days under refrigeration (+2 °C + 8 °C) in amber glass vials. However, alcohol is not recommended for use in pediatric therapeutics or is used at a percentage of less than 5% [5]. Moreover, sodium benzoate can induce neonatal icterus [6].

To avoid these excipients with known effects, we decided to rely on a commercial compounding vehicle: Syrspend® SF PH4, a product that is frequently used in oral suspension drugs. Many studies have approved the compatibility between active pharmaceutical ingredients (API) and this vehicle [7, 8].

Furthermore, the stability of prednisolone suspension (Figure 2) in Syrspend® SF PH4 was studied [8], while it remains unknown for prednisone.

Materials and methods

Analytical method

Reagents

Micronized prednisone was bought to Inresa (Bartenheim, France) and Syrspend® SF PH4 to Fagron

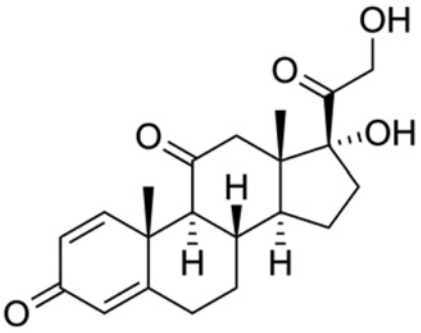


Figure 1: chemical structure of prednisone.

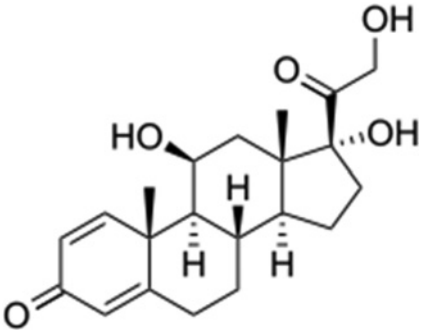


Figure 2: chemical structure of prednisolone.

(Thiais, France). Methanol was of HPLC grade and was purchased from VWR Chemicals (Fontenay-sous-Bois, France). Prednisone and prednisolone standards were procured from Merck (Darmstadt, Germany).

Water for HPLC was distilled and passed through a reverse osmosis system. Hydrochloric acid (HCl) solutions 0.1 M and 1 M were purchased from VWR Chemicals (Fontenay-sous-Bois, France), sodium hydroxide (NaOH) 0.1 M and 1 M were bought to Merck (Darmstadt, Germany), oxygen peroxide (H_2O_2) 10 volumes was acquired from Gifrer (Decines-Charpieu, France).

Instrumentation and chromatographic conditions

The HPLC system included a 717 plus autosampler, 2487 UV detector, and a HPLC 515 pump (Waters, Milford, USA). Chromatographic separation of the analytes was carried out on Waters Xterra RP C18 5 µm column (4.6*150 mm). The volume injection of the sample was 10 µL. The flow rate was kept at 1 mL/min and prednisone was detected at 254 nm [9, 10]. The oven temperature was kept at 45 degrees Celsius.

Multiple mobile phases were tested to achieve an optimal elution. Fourteen different combinations of organic solvent and water were tried: acetonitrile/water, acetonitrile/methanol/water and methanol/water, each at various proportions.

Data were acquired and processed with EMPOWER Software (Warers, Milford, USA). All calculations were performed using Microsoft Excel 2010 (Microsoft Corporation, USA).

Preparation of oral suspensions

Three batches of 5 mg/mL oral suspension were prepared, using 350 mg of micronized prednisone and 70 mL of Syrspend® SF PH4. These were packaged in amber glass vials (60 mL) to protect from light and stored at room temperature throughout the study. According to the European Pharmacopoeia [11], prednisone could be protected from light. That why, the study was realized with amber glass.

Prednisone concentrations were determined on days 0, 1, 4, 10, 30, 60, 90 after the first day of production.

Method parameters validation

The HPLC method was validated according to the International Conference on Harmonization (ICH) guidelines (Q2R1) [12] including the assessment of system linearity, accuracy, precision (repeatability, intermediate precision) and specificity [13].

Standard stock solutions of prednisone were prepared in methanol to obtain a concentration of 5 mg/mL. Six calibration curves were prepared using this solution. The work concentrations of calibration standards were 75 µg/mL, 100 µg/mL, 125 µg/mL, 150 µg/mL and 175 µg/mL and the work concentrations of the three quality controls (QC) were 75 µg/mL, 125 µg/mL and 175 µg/mL. An assay range between 60 % and 140 % of the target value (125 µg/mL) was respected according to the ICH.

Linearity

The response function was performed on three different days with the six calibrations curves. In order to check whether an excipient effect existed, two types of ranges were produced: a range only containing the API and a reconstituted range, with Syrspend® SF PH4. The method

was considered as linear if the coefficient of determination was over 0.99 for the mean standard curve.

Accuracy

The accuracy was determined using the data obtained during study of the response function. For each QC, the accuracy was measured by calculating the report between theoretical and calculated concentrations. This report allows the access to a recovery rate, whereby, it had to be less than 5% in order to be accepted.

Precision

To determine the repeatability of this method, six points of the middle of the range was performed (125 µg/mL), and each point was prepared by independent weighing. Then, the intermediate precision was determined on three different days, using the relative standard variation (RSD), which had to be less than 5%.

Stability indicating method

A stability indicating method is a process that is able to distinguish the API from its degradation products. The method has to be sufficiently sensitive to detect these degradation products in low quantity and sufficiently resolute to distinguish products with potentially close structures [13, 14].

Forced degradation experiments were carried out on prednisone under various conditions explained in the ICH guideline: heat, acid, alkaline and oxidative conditions.

A thermal degradation study was performed at two different temperatures: room temperature (24 °C ± 1 °C) and 80 °C in a water bath. The exposure time was one hour in both conditions.

Acid hydrolysis was studied by adding HCl solutions at 0.1 M, 0.5 M and 1 M in prednisone solution. At one hour of exposure time, neutralization was performed with respectively 0.1 M, 0.5 M, and 1 M NaOH solutions. The alkaline hydrolysis was performed by doing the opposite procedure of acid hydrolysis (exposition with NaOH, then neutralization with HCl). Acid and alkaline degradation was performed in a water bath heated to 80 °C, for one hour.

Oxidative degradation was assessed by exposed prednisone solution in 10 volumes of H_2O_2 for three hours in a water bath heated to 100 °C.

The degradation was confirmed if a reduction of more 5% of prednisone concentration was observed.

Related substances

A solution of prednisolone was prepared in methanol to obtain a concentration of 5 mg/mL to differentiate prednisone to prednisolone. A work concentration of 125 µg/mL of prednisolone was compared to the same concentration of prednisone solution by HPLC. The same analysis method was used for the two molecules.

The resolution between these two peaks had to be more than 1.5 to validate the separation.

Analysis during the studied period

Three prednisone oral suspensions were prepared at day 0. During each time of the study (days 0, 1, 4, 10, 30, 60, 90) physical and chemical parameters were observed on the three batches.

Visual and odour inspection

A visual inspection was done in order to detect precipitation or variation of colour with time. A control of odour suspension was also performed.

Osmolality

The osmolality of the suspension was measured with Advanced Instruments Model 3250 Osmometer (Radiometer, Neuilly-Plaisance, France). A 250 µL aliquot of each suspension were taken and diluted (1:2 v/v) in water for injection before measurement.

pH

The pH was determined with a pH-meter: pHenomenal VWR® (VWR Chemicals, Fontenay-sous-Bois, France).

Measure of concentration

Prednisone concentration was quantified in triplicates immediately after preparation and after 1, 4, 10, 30, 60 and 90 days. Before removing samples, the containers

were handshaken manually to ensure a homogeneous suspension, according to the 9th edition of the European Pharmacopoeia [11]. Then, 400 µL sample of each preparation was diluted (1:10 v/v) in methanol and centrifuged at 4000 rpm for five minutes to sediment insoluble excipients. Another dilution (1:4 v/v) of supernatant was performed in methanol for HPLC analysis. The chemical stability was determined by calculating the percentage of the initial concentration remaining at each time interval: prednisone concentration in subsequent samples greater than 95 % were considered stable.

Statistical and data analysis Statistical tests were performed by Excel® software (Microsoft Office, USA, 2007) with a risk α set at 5 %. Statistical significance was specified as $p < 0.05$.

Before using the Student t-test, the Shapiro-Wilk test was performed to show a normality test data ($\alpha = 0.05$).

Results

Analytical method

The chosen mobile phase has been composed of methanol/water (45:55 v/v).

Method parameters validation

Linearity

The coefficients of determination were 0.9999, 0.9994 and 0.9998, for days 1, 2 and 3, respectively, in the suspension without Syrspend® SF PH4.

For the suspension with Syrspend® SF PH4, the coefficients of determination were 0.9999, 0.9999 and 0.9998, for days 1, 2 and 3, respectively.

The average of regression equations was without and with Syrspend® SF PH4: $y = 22096x\text{-}1129$ ($r^2 = 0.9997$) and $y = 22791x\text{-}35{,}573$ ($r^2 = 0.9998$), respectively. Student statistical test did not show significant differences between the slopes and the y-intercepts ($\alpha = 5\,\%$). No excipient effect was observed between curves with and without Syrspend® SF PH4.

Accuracy

The accuracy rates for the 75 µg/mL, 125 µg/mL and 175 µg/mL QC were estimated to be 0.50 %, 0.59 % and 1.12 %, respectively. These results related to ranges with excipient.

Precision

This method is repeatable because of a RSD of 1.64 %, 2.16 % and 1.37 %, for days 1, 2 and 3, respectively.

The results of the intermediate precision for three days showed a RSD of 1.72 %.

Stability indicating method

No degradation was observed at room temperature (20 °C) (Figure 3) and heating at 80 °C (Figure 4).

The acid hydrolysis showed a reduction of prednisone concentration of 8.7 % with HCl 1 M (Figure 5). No degradation was observed with 0.1 and 0.5 M of HCl (0.8 % and 4 % respectively).

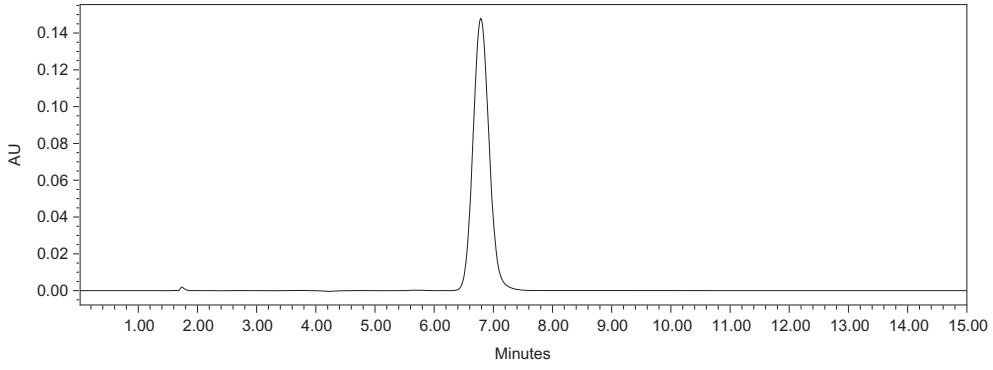


Figure 3: chromatogram of prednisone at room temperature.

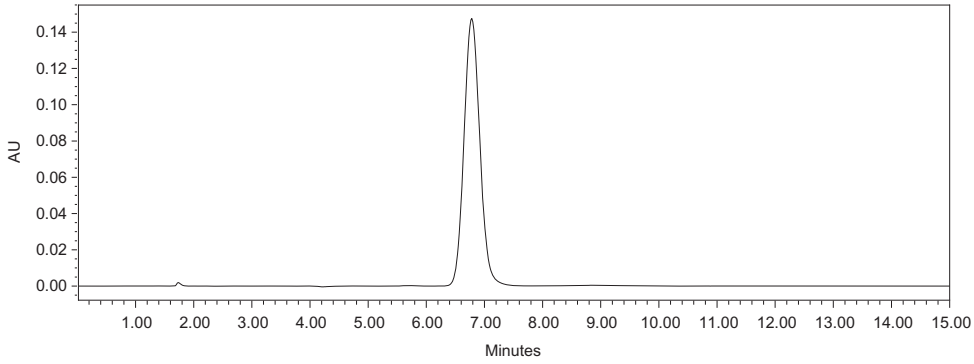


Figure 4: chromatogram of prednisone heating at 80 °C.

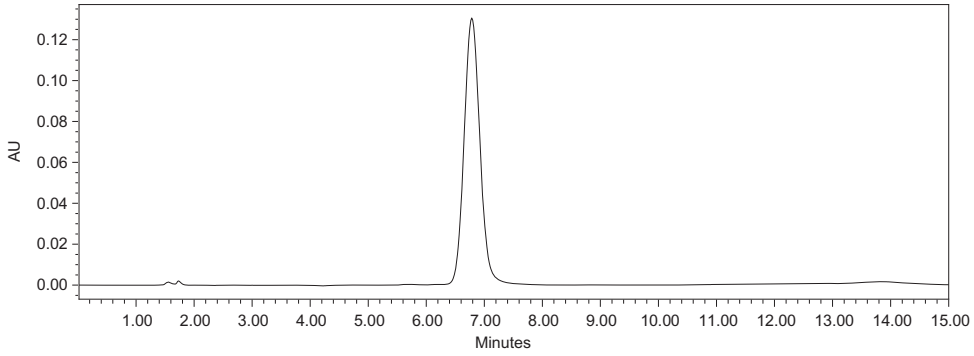


Figure 5: chromatogram of prednisone and products of degradation with HCl 1 M.

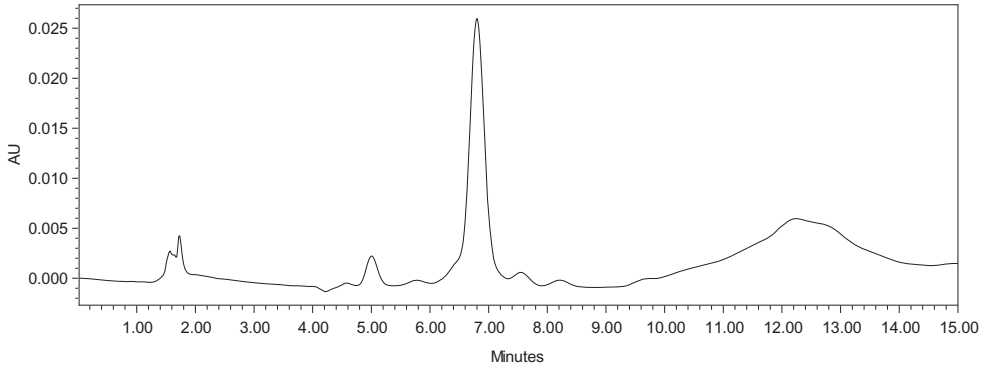


Figure 6: chromatogram of prednisone and products of degradation with NaOH 0.1 M.

The alkaline hydrolysis was observed with low concentration of NaOH. In fact, a reduction of 80 % of prednisone concentration was visible with NaOH 0.1 M (Figure 6). The same result was noted with 0.5 and 1 M of NaOH.

No variation was observed with H_2O_2 (reduction of 4.5 %).

The prednisone degradation is poor in acid environment but major in basic environment.

Related substances

The resolution between peaks of prednisone and prednisolone was calculated at 2.9 (Figure 7).

Analysis during the studied period

Visual and odour inspection

No precipitation, no variation of colour or odour on the suspension was observed in the three batches.

Osmolality

During the study period, all osmolality measurements were included between 42 and 46 mOsm/Kg (Table 1). No significant variation of osmolality was observed.

pH

During the study, all pH measurements were included between 4.18 and 4.22 (Table 1). No significant variation of pH was observed.

Measure of concentration

After validation of the analytical method, prednisone concentrations remained stable within more or less 5% of nominal value over 60 days. Two of the three batches showed a concentration more than 5% of nominal value on the day 90 (Table 2). Results of the Shapiro-test showed that samples followed a normality test data (p-value = 0.9638). Student test did not show a significant difference from day 0 to day 60 (t calc < t table). However, a significant difference from the day 90 was observed (t calc = 5.3 and t table = 2.92).

Discussion

A suspension of prednisone dosing at 5 mg/mL in Syrspend® SF PH4 was tested using a simple method: high performance liquid chromatography (HPLC).

After the fourteen tests, the mobile phase methanol/water (45:55 v/v) seemed more efficient than the other mixtures: the retention time was optimal (approximately seven minutes) and the peak was optimal (tailing factor = 1.1). Other mixtures that could have been tested were various combinations of methanol/water/tetrahydrofuran [15, 16].

The chemical structure of prednisone is similar to the prednisolone structure. The difference is the molecular

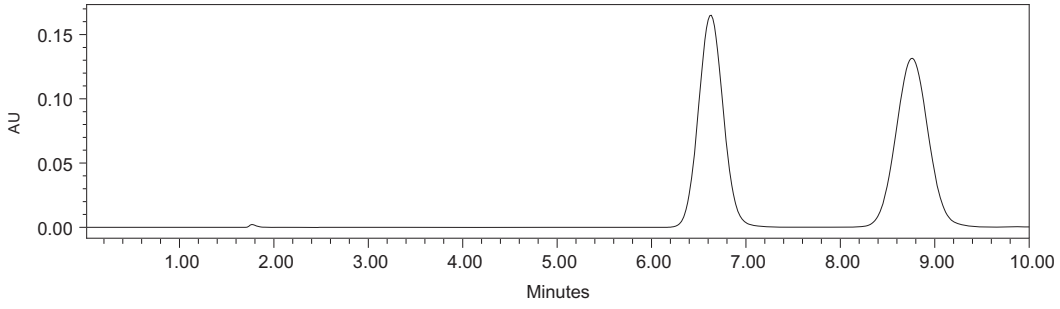


Figure 7: chromatogram of prednisone (on the left) and prednisolone (on the right).

Table 1: pH and Osmolality values of prednisone in oral suspension. pH and Osmolality expressed as mean ± standard deviation (SD) of triplicate measurements of one test suspension (n = 3).

	Day 0	Day 1	Day 4	Day 10	Day 30	Day 60	Day 90
pH	4.22 ± 0.02	4.21 ± 0.00	4.21 ± 0.01	4.19 ± 0.01	4.19 ± 0.01	4.19 ± 0.01	4.18 ± 0.00
Osmolality	42.67 ± 1.15	46.00 ± 0.00	42.00 ± 2.00	44.67 ± 1.15	44.00 ± 2.00	43.33 ± 2.31	44.67 ± 3.06

Table 2: concentration of prednisone in oral suspension over 90 days. Concentration expressed as mean ± RSD of triplicate assays of one suspension (n = 3).

Test solution	Drug concentration in sample (mg/mL)		% initial concentration remaining ± relative deviation standard (RSD)					
	Nominal	Day 0	Day 1	Day 4	Day 10	Day 30	Day 60	Day 90
A	5	4.76 ± 0.08	97.0 ± 0.1	99.4 ± 2.0	96.6 ± 2.0	98.4 ± 0.5	97.1 ± 0.9	95.4 ± 0.2
B	5	4.94 ± 0.02	95.4 ± 0.1	95.6 ± 1.3	97.5 ± 0.7	97.3 ± 0.1	98.1 ± 1.7	94.4 ± 0.6
C	5	4.96 ± 0.03	96.6 ± 0.3	103.0 ± 2.9	97.9 ± 0.2	99.5 ± 0.4	97.4 ± 1.1	94.8 ± 0.9

Note: drug concentration in samples taken at time zero was designated as 100 %.

chemical group on the Carbon number 12: an alcohol group is substituted by a ketone group in prednisolone. A chromatographic separation of prednisone and prednisolone confirmed that the retention time of these two molecules are different.

The validation of the analytical method confirmed the use of this method to measure the concentration of prednisone with HPLC. A good linearity with a coefficient of determination constantly more than 0.999 was obtained. The accuracy and the precision rates were measured to be less than 5 %, suggesting that this method is highly repeatable. The stability indicating method has permitted to bring out degradation products of prednisone [13].

The study of prednisone suspension in Syrspend® SF PH4 showed a stability of 60 days. Any variation of pH measurement and osmolality measurement was observed. Concentrations of prednisone remained stable within more or less 5 % of nominal values over 60 days. No degradation product was detected throughout the studied period.

A variation of concentration is fixed to 5 % for drugs with narrow therapeutic window, and 10 % for other therapeutic [13]. Even if prednisone is not a drug with narrow therapeutic window, we preferred to secure the reduction of concentration to 5 % of the nominal values because this suspension is reserved for children.

The microbiological stability is recommended to show the conservation over time within limits for contamination (ie: germs, moulds, yeasts) as according to the European Pharmacopoeia [12, 14]. However, the microbiological stability of this suspension was not evaluated because of lake of materials in the laboratory.

Viscosity analysis is a limit of this study [13]. The friction force was not evaluated because no rotating viscometer was available in our laboratory.

Taken together, the results of this study showed that this new suspension is easier to produce than the syrup of prednisone with alcohol, sodium benzoate and simple syrup. Indeed, the fabrication time is shorter and the number of compounds is smaller.

Conclusion

This study showed that 5 mg/mL prednisone oral suspension in Syrspend® SF PH4 was stable for 60 days, at room temperature and protected from light. This new suspension would provide an interesting alternative to the syrup with alcohol and sodium benzoate, especially for pediatric use.

Conflict of interest statement: Authors state no conflict of interest. All authors have read the journal's Publication ethics and publication malpractice statement available at the journal's website and hereby confirm that they comply with all its parts applicable to the present scientific work.

References

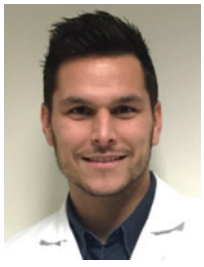
1. Résumé des caractéristiques du produit. 2011 1–6. Available at: http://agence-prd.ansm.sante.fr/php/ecodex/rcp/R0186846.htm. Accessed 3 Nov 2017.
2. Das Gupta V, Gibbs CW, Ghanekar A. Stability of pediatric liquid dosage forms of ethacrynic acid, indomethacin, methyldopate hydrochloride, prednisone and spironolactone. Am J Heal Pharm. [Internet]. 1978;35 Available at. http://www.ajhp.org/content/35/11/1382.short?sso-checked=true. Accessed 5 Dec 2017.
3. Friciu M, Plourde K, Leclair G, Danapoulos P, Savji T. Stability of prednisone in oral mix suspending vehicle. Int J Pharm Compd. [Internet]. 2015;19:337. Jul 1. http://www.ijpc.com/Abstracts/Abstract.cfm?ABS=4023. Accessed 5 Dec 2017.
4. Schlatter J, Brion F. Préparations orales liquides en pédiatrie : le guide. Lavoisier; 2015.
5. Saviuc P, Castot A, Lerebours S, Bidault I, Cabot C, De Haro L, et al. Comite de coordination de toxicovigilance. 2006.

Available at: http://www.centres-antipoison.net/CCTV/rapport_ethanol_CCTV_2006.pdf. Accessed 3 Nov 2017.
6. AFSSAPS. Liste des Excipients à Effet Notoire. [Internet]. 2009;1–84. Available at: http://ansm.sante.fr/var/ansm_site/storage/original/application/29aa941a3e557fb62cbe45ab09dce305.pdf. Accessed 3 Nov 2017.
7. SyrSpend® SF PH4 LIQUID | Fagron France [Internet]. Available at: https://fr.fagron.com/fr/product-innovations/syrspendr-sf-ph4-liquid. Accessed 3 Nov 2017.
8. Geiger CM, Sorenson B, Whaley P. Stability assessment of 10 active pharmaceutical ingredients compounded in syrspend SF. Int J Pharm Compd. [Internet]. 2015;19:420–27. Available at: http://www.ijpc.com/Abstracts/Abstract.cfm?ABS = 4050. Accessed 3 Nov 2017.
9. Lake BR, Chemist PA, Romesberg R, Chemist HA, Wittrig M, Chemist D. Superior separations of unsaturated compounds by HPLC. Baseline. 2005;4:2–3.
10. Kwak HW, D'Amico DJ. Determination of dexamethasone sodium phosphate in the vitreous by high performance liquid chromatography. Korean J Ophthalmol. [Internet]. 1995;9:79. Available at. http://www.ncbi.nlm.nih.gov/pubmed/8818321%0Ahttps://synapse.koreamed.org/DOIx.php?id = 10.3341/kjo.1995.9.2.79.
11. Pharmacopée européenne 9ème édition 9.0, 9.1, 9.2: : 9789287181329 Edqm/conseil de l'europe, Gestion - Règlementation [Internet]. 2017 Available at: https://www.unitheque.com/Livre/edqm_-_conseil_de_l_europe/Pharmacopee_europeenne_9eme_edition_9.0_9.1_9.2-97053.html#gallery-1. Accessed 16 Nov 2017.
12. ICH Expert Working Group. ICH guideline Q1A(R2) stability testing of new drug substances and products. In: International Conference on Harmonization [Internet]. 2003 p. 24. Available at: http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q1A_R2/Step4/Q1A_R2__Guideline.pdf. Accessed 5 Nov 2017.
13. Sautou V, Bossard D, Chedru-Legros V, Crauste-Manciet S, Fleury-Souverain S, Lagarce F, et al. Methodological guidelines for stability studies of hospital pharmaceutical preparations [Internet]. 2013 Available at: https://www.gerpac.eu/IMG/pdf/guide_stabilite_anglais.pdf. Accessed 5 Nov 2017.
14. Blessy MN, Patel RD, Prajapati PN, Agrawal YK. Development of forced degradation and stability indicating studies of drugs—A review. J Pharm Anal. [Internet] 2014;4:159–65. Available at: https://ac.els-cdn.com/S2095177913001007/1-s2.0-S2095177913001007-main.pdf?_tid = b1bbeb08-c257-11e7-bab9-00000aab0f26&acdnat = 1509906936_0e9bbad999642cfd5dfd6ce9424a2006. Accessed 5 Nov 2017.
15. Williamsx PA, Biehl ER. High-pressure liquid chromatographic determination of corticosteroids in topical pharmaceuticals. J Pharm Sci. 2017;70:530–34. [Internet]. DOI:http://dx.doi.org/10.1002/jps.2600700517.
16. Lou H, Liu M, Wang L, Mishra SR, Qu W, Johnson J, et al. Development of a mini-tablet of co-grinded prednisone-Neusilin complex for pediatric use. AAPS PharmSciTech. [Internet]. 2013;14:950–58. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23761262. Accessed 8 Nov 2017.

Bionotes

Anne-Claire Bonnaure
CHU de Rennes, 2 rue Henri Le Guilloux, 35000 Rennes, France, **anne-claire.bonnaure@hotmail.com**

Anne-Claire Bonnaure After graduating from the Faculty of Pharmacy at the University of Rennes1, Anne-Claire Bonnaure chose a hospital career and became resident pharmacist in 2014. She spent her residency in the University Hospital and the Anticancer Centre of Rennes, and in the Hospitals of Lorient and Saint-Brieuc in Brittany (France). Her interests in the field of pharmaceutical technology include quality control units and chemotherapy production.



Romain Bellay
CHU de Rennes, 2 rue Henri Le Guilloux, 35000 Rennes, France, **romain.bellay@hotmail.fr**

Romain Bellay is currently a pharmD candidate working at the Pharmacy Department of the University Hospital of Rennes, France. In 2017, he obtained his university degree in clinical pharmacy. In the field of pharmaceutical technology his special interests include new oral formulations, quality control as well as physicochemical stability of drug suspensions.

Pauline Rault
CHU de Rennes, 2 rue Henri Le Guilloux, 35000 Rennes, France, **pauline.rlt@gmail.com**

Pauline Rault, pharmD candidate, has two years of internship left before her graduation. Currently working at the sterilization ward of the Rennes University Hospital, she is also specializing in pharmacoeconomics thanks to the Paris Descartes' diploma. Her last semester in paediatric nutrition allowed her to conduct a stability study of vitamin formulations. In the meantime, she is teaching pharmacology to students at Pharmacy University and at nursing school.

Marie-Antoinette Lester
Marie-Antoinette Lester is a hospital pharmacist at Rennes University Hospital. Since 2006 she has been senior pharmacist involved in sterile preparations (cytotoxic and parenteral nutrition) and unsterile preparations. She became head of the pharmaco-technology unit in 2014.

Pierre-Nicolas Boivin
CHU de Rennes, 2 rue Henri Le Guilloux, 35000 Rennes, France,
pierre-nicolas.BOIVIN@chu-rennes.fr

Pierre-Nicolas Boivin is a hospital pharmacist in the manufacturing and quality control laboratory at the Pharmacy Department of the University Hospital of Rennes. His work is focused on sterile preparations (cytotoxic, eye drops and parenteral nutrition) and unsterile preparations. He is involved in the development and validation of analytical methods and implementation of stability studies.