RESEARCH ARTICLE

Formulation of povidone iodine toothpaste and evaluation of its chemical stability

Abdel Naser Zaid

Department of Pharmaceutics and Pharmacokinetics, School of Pharmacy, An-Najah National University, Nablus, Palestine

The aim of this study is to formulate a toothpaste containing povidone-iodine (PVP-I) and evaluate its chemical stability. PVP-I was incorporated into toothpastes from different trademarks and a new toothpaste formulation containing PVP-I was also prepared. The obtained toothpastes were coded as F1, F2, F3 and F4, respectively. Chemical stability of PVP-I in the formulations (according to the USP method) was checked over a period of 7 weeks. Color, pH and smell of the obtained toothpaste formulations were evaluated. PVP-I in F1, F2 and F3 toothpastes was stable over the 7-week period in the first two formulations and for only 4 weeks in the last one. However, PVP-I was only stable for a period of 3 weeks when it was the only active ingredient as in F4. The pH of the formulations remained constant for the entire study period for all formulations. No changes in viscosity, smell or color of all the toothpaste formulations were observed. The compounding of PVP-I toothpaste in order to achieve oral hygiene can be achieved successfully. Attention should be made by practicing pharmacists with regard to the exact expiry dates of the obtained formulations.

Key words: *Compounding, PVP-I, stability, toothpaste*

INTRODUCTION

Povidone-iodine (PVP-I) is a stable chemical complex of polyvinylpyrrolidone and elemental iodine [Figure 1].

It contains from 9.0% to 12.0% available iodine, calculated on a dry basis.[1] It has been demonstrated that bacteria do not develop resistance to povidone-iodine (PVP-I).[2,3] Consequently, PVP-I has found broad application in medicine and thus, it has been formulated at concentrations of 7.5-10.0% in forms of solutions, sprays, surgical scrubs, ointments, as well as swabs for pre- and post-operative skin cleansing in both treatment and prevention of infections in wounds, ulcers, cuts and burns. In addition, utilization of PVP-I was found to be potentially beneficial in the management of some periodontal diseases.[4] In fact, oral solutions containing 7.5% PVP-I are available in pharmacies as mouth gargles for the treatment of viral and bacterial throat and mouth infections.[5] Furthermore, Shiraishi *et al*, encouraged the use of the PVP-I gargle, since it contributes to reduction in absence rates from school and work due to common colds and influenza, indicating that gargling with PVP-I is useful for the prevention from these two diseases.[6]

Address for correspondence:
Dr. Abdel Naser Zaid,
Department of Pharmaceutics and Pharmacokinetics,
School of Pharmacy, An-Najah National University,
P.O. Box: 7, Nablus, Palestine.
E-mail: dal_naser@yahoo.com

Therefore, the formulation of PVP-I as a toothpaste may be a good tool for routine oral hygiene and protection from contaminants and several pathogenic microorganisms. In fact, from a hygienic point of view, the availability in the of such formulations in the market provides a selection of interesting products for personal oral hygiene. Unfortunately, PVP-I formulated as a toothpaste is not available in the cosmeceutical market. Therefore, it would be interesting if the pharmacist can prepare or reformulate this potent antiseptic into a toothpaste in order to achieve better therapeutic outcomes in the treatment and prevention of throat and mouth infections. This study aims to compound a new toothpaste formulation containing PVP-I, and

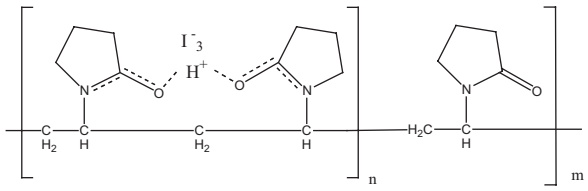

Figure 1: Structure of povidone-iodine

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also to incorporate it into toothpastes already present on the market and then evaluate the chemical stability of PVP-I in the obtained formulations.

MATERIALS AND METHODS

Chemicals

All chemicals and reagents were USP/NF or ACS grade and were used without further purification. PVP-I powder was purchased from Medichem (Hon, China), sodium thiosulfate was obtained from Riedel-de Haen Ag (Seelze, Germany), Sodium lauryl ether sulfate (Texapon), calcium orthophosphate, glycerin, methyl cellulose, sodium saccharine and menthol were supplied by Sun Pharamaceuticals (Nablus, Palestine). All toothpastes were bought from community pharmacies and supermarkets. The products were valid for at least 1 year from the date of testing.

Equipment

All pH values were measured using a pH 211 microprocessor pH meter from Hanna Instruments (Woonsocket, Rhode Island), and an electrical Laboratory balance (Type AEy-20G Shimidazu Corp. Japan). For purified and distilled water, a Reverse Osmosis (R.O.) water system (model HP-300 Cuno/ water factory system / USA) was used.)

Preparation of formulations

Preparation of a new PVP-I toothpaste formulation

This toothpaste was completely formulated according to the following Table and it was coded as F4.

Incorporation of PVP-I into trademark toothpastes and preparing new formulations

Sample preparations for stability studies were prepared using the levigation method: Disperse 7.5 grams of PVP-I in 7.5 g of the selected toothpaste at room temperature until obtaining a homogenous dispersion (Mixture I). Add another 15 g of toothpaste to mixture I and levigate slowly until obtaining a homogenous paste (paste II). Add another 30 g of toothpaste to paste II and repeat levigation to obtain paste III. Add the remaining amount of toothpaste to paste III to achieve a total of 100 g of the final formulation and repeat the levigation step. Fill in opaque plastic tubes. The obtained new toothpastes were coded as F1, F2 and F3. All blank and active drug formulations were prepared in duplicates and stored in 100-cc opaque plastic jars. Preparations were stored at 25°C (room temperature). Each toothpaste formulation was visually assessed for color and smell before it was poured into the jars. The jars were labeled as 7.5% toothpaste and blank formulation. Approximately 5 g of formulation from each jar, and from the blank formulation, were taken for chemical analysis and apparent pH measurement. The samples were taken at 0, 1, 2, 3, 4, 5, 6 and 7 weeks for F1 and F2 and at 0, 1, 2, 3 and 4 for F3 while analysis was stopped at week 3 for the F4 formulation. All samples were tested for pH and analyzed for PVP-I concentrations.

Preparation of blank solutions

Blank toothpastes were prepared in the same manner as described in Table 1, but without the use of PVP-I. Blank formulations were labeled as blank toothpaste.

Analytical method

Assay of available iodine

To establish the PVP-I content in the prepared formulations, standard and samples were analyzed using the official analytical method of the USP.

Titration conditions

The 0.02 N VS sodium thiosulfate was prepared by dissolving 3.16 g of sodium thiosulfate in 1000 ml distilled water. PVP-I concentrations were determined using the titration method described in the USP as follows: Transfer an accurately weighed quantity of toothpaste equivalent to 50 mgs of iodine to a 100-ml beaker, add water to make a total volume of not less than 30 ml, and stir until the complete dissolution of the formulations. Titrate immediately with 0.02 N sodium thiosulfate VS, determining the end point visually by the use of starch solution as indicator as reported by Jayaraj Kumar.[7] Perform a blank determination, and make any required correction. Each ml of 0.02 N sodium thiosulfate is equivalent to 2.538 mg of available iodine. The color of the solution at the end point is that of the blank solution. The volume of sodium thiosulfate solution utilized in both methods was equal which may suggest that the two methods are interchangeable.

RESULTS

Chemical stability

The assay method used for this study was reported by the USP. The same method was also conducted with a variation in the determination of the end point of the titration.[7] In this last modification, starch solution was used for the determination of the end point. No differences in the assay were observed between the two methods. This suggests the use of this last method in the lab whenever a potentiometer

Table 1: Formulation of 7.5% PVP-I_2 tooth paste

Ingredient	Quantity (grams)
Tricalcium phosphate	30.0
PVP-I	7.5
Texapon (sodium lauryl ether sulfate)	4.0
Glycerin	20
Methyl cellulose	1.5
Sodium saccharine	0.40
Menthol	1.0
Purified water	up to 100

Procedure of mixing:
1. Triturate PVP-I, menthol and tricalcium phosphate on an ointment tile (Mixture I).
2. Disperse Texapone in glycerin
3. Dissolve sodium saccharine in water and mix this solution with the above dispersion (Mixture II).
4. Levigate mixture II with mixture I until obtaining a final homogeneous toothpaste.
5. Fill this toothpaste in a plastic jar and code it as F4.

is not available. The chemical stability of the novel PVP-I 7.5% toothpaste formulation and the formulations where PVP-I was incorporated into trademark toothpastes stored in opaque plastic jars at room temperature is summarized in Table 2. As expected, the rate of degradation of PVP-I in the above formulations varied due to the different components present in each one [Table 3]. After 7 weeks, the available iodine in the compounded toothpastes (F1) and (F2) was within the accepted range of the USP for PVP-I for cleansing solution[1] (85-120). PVP-I in the third toothpaste (F3) was below the accepted level after only 4 weeks of storage, while toothpaste formulation (F4) was chemically stable till the end of the third week of storage as reported in table 2. The r^2 of these results are close to 1 which indicates a good correlation between the assay measurement and the predicted values. Therefore, these formulations can be used within this time limit.

Apparent pH and physical appearance

The pH's of the re-compounded toothpastes were within the accepted range described in the USP for PVP-I solution. These pH values remain constant within the entire period of stability study for all formulations with F1and F2 having pH of 4.5 and 4.3, respectively while F3 and F4 have pH values of 7 and 6.3, respectively. Concerning the appearance of the prepared PVP-I toothpastes, no detectable changes in the obtained odor, color or precipitate were observed at the end of the study.

DISCUSSION

As expected from the obtained results, the compounded PVP-I 7.5% toothpastes, prepared and stored at room temperature, had different rates of degradation for PVP-I. In fact, F1 and F2 were chemically stable for more than 7 weeks, while PVP-I in formulation (F3) was chemically stable for only 4 weeks when stored at the same conditions. The last one (F4) toothpaste was stable for only 3 weeks when stored at the same conditions. These results were expected since these formulations are different and contain different components as shown in Table 3. In fact, F1 and F2 were gel toothpastes and do not contain calcium salts and the pH of the obtained formulations were 4, 5 and 4.3, respectively while the F3 and F4 contained calcium salts and had pH values of 7 and 6.3, respectively. This may suggest an effect of calcium ions and pH in the degradation rate of PVP-I while the fluoride ion should not influence this rate of degradation, since it was not introduced in F4 which showed only 3 weeks of stability at room temperature. But further study is required to evaluate the impact of PVP-I on fluoride stability and efficacy since this ion plays an important role in the prevention of tooth decay and results in cavities.

The obtained stability results suggest that these formulations may be suitable for incorporating PVP-I into toothpastes for pharmaceutical purposes, but attention should be made to determine the exact and true expiry date beyond which the consumer should discard the remaining amount of the compounded formulation. This may encourage consumers to use this potent antiseptic for oral disinfection especially when the expiry date of the obtained formulation is long as in the case of the first two toothpastes (F1 and F2). In addition, the field of cosmeceuticals should pay attention to this study since it may offer another important market option for this industry. In fact, these industries may develop and produce new stable toothpaste formulations containing this potent antiseptic for oral hygiene or as a medication for patients who have oral or gingival infections. Community pharmacists may also benefit from these results, since they can formulate PVP-I in an existing toothpaste to meet consumers' desire, especially those who are not willing to change their personal or favorite toothpaste but are still looking for the ideal antiseptic to achieve higher therapeutic benefits when they are suffering from gingivitis or minor aphthous ulcers which compounds 80% of all aphthae and heals in 7-14 days.[8] In this context, the pharmacist could search for a stable PVP-I toothpaste not only for oral hygiene as previously mentioned, but also for patients having infections that respond to PVP-I in the oral cavity.

Table 2: Percentage of available PVP-I in different toothpastes at 25°C

Time (Weeks)	% of available iodine ± RSD (*n*=3)			
	F1	F2	F3	F4
0	102.0±1.1	101.2±1.7	101.1±1.3	101.0±1.1
1	99.5±1	100.0±1.5	99.5±0.7	94.3±1.2
2	97.3±1.2	98.1±1.4	97.2±09	90.6±0.9
3	96.5±0.9	95.2±1	95±1	85±1
4	95.8±1.4	94.0±1.1	91.7±1.1	*
5	94±1.6	93.2±	*	*
6	93±1.3	92.4±	*	*
7	90±0.8	90.8±	*	*
r^2	0.969	0.9678	0.9846	0.9889

r^2=r-squared; *n*=number of analysis performed for each test; RSD=relative standard deviation; *=analysis is not performed at this period

Table 3: Composition of trademark toothpastes

Toothpaste	Composition
F1	Sodium fluoride, sorbitol, hydrated silica, sodium lauryl sulfate, PEG-32, aroma, cellulose gum, sodium saccharine, mic, glycerin, menthol, limonene, CI 19140, CI 42090, CI 77891.
F2	Sodium fluoride, sorbitol, hydrated silica, sodium lauryl sulfate, aroma, PEG-12, cellulose gum, cocamidopropyl betaine, sodium saccharine, hydroxyl methyl cellulose, menthol, limonene, CI 42090, CI 74160, CI 77891.
F3	Sodium fluoride, calcium carbonate, aqua, sorbitol, hydrated silica, sodium lauryl sulfate, aroma, cellulose gum, potassium citrate, trisodium phosphate, sodium saccharine, calcium glycerophosphate, phenyl carbinol, glycerin CI 74260.

CONCLUSIONS

According to stability results obtained in this study, the practice of compounding PVP-I in various trademark toothpastes in order to achieve oral disinfection benefits can be followed in community pharmacies, but further studies should be conducted in order to investigate the impact of PVP-I on other therapeutic ingredients present in toothpaste formulations. Additionally, further investigation should be carried out to confirm the clinical efficacy of this combination in oral hygiene. Attention should also be taken to evaluate the true shelf life of the obtained formulations.

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