The Thai Journal of Pharmaceutical Sciences

Volume 15
Issue 4 *1990*

Article 2

1-1-1990

Antimicrobial Activity of p-Aminobenzoic Acid and Its Application as a Preservative in Pharmaceutical Products(ฤทธิ์การต้านจุลชีพของพารา- อะมิโนเบนโซอิคแอซิดและ...

Malyn Chulasiri

Michael E. Richards

ปฐมนิพนธ์

ORIGINAL ARTICLE

Antimicrobial Activity of p-Aminobenzoic Acid and Its Application as a Preservative in Pharmaceutical Products

*Malyn Chulasiri Ph.D.**

Michael E. Richards Ph.D., DSc. **

Abstract

p-Aminobenzoic acid (PABA) showed inhibitory effect upon *Staphylococcus aureus* NCTC 10788, *Pseudomonas aeruginosa* NCTC 6750, *Escherichia coli* NCTC 8110 and *Candida albicans* NCPF 3179. Its antimicrobial activity was affected by different solvent system and pH. The better activity was observed when PABA was dissolved in alcohol and lowering of pH increased its inhibitory effect. Also, in the presence of sodium metabisulfite, the activity of the compound increased. After 3 months of storage at room temperature, PABA solution still maintained its inhibitory effect upon the test microbial strains. When this agent, at 0.5%, was added in morphine mixture and frusemide suspension, it was able to inactivate the aforementioned microorganisms within 6 hours after inoculating those microbial strains into the products. (Th. J. Pharm. Sci., Vol. 15 No. 4, 243-253 (1990))

Key Words : p-Aminobenzoic acid, PABA, preservative.

* Department of Microbiology, Faculty of Pharmacy, Mahidol University, Bangkok 10400, Thailand.

** School of Pharmacy, Robert Gordon's Institute of Technology, Aberdeen AB9 1FR, Scotland.

Introduction

It is clear that non-sterile aqueous pharmaceuticals especially those taken orally must be preserved, but the criteria that any acceptable preservative must be fulfilled severely limits the available choice. There are many factors govern the choice of a suitable preservative, e.g., the compound must be soluble and compatible in the formulation; biological activity should be unaffected by either the active ingredients or other excipients of the preparations, but the major factors are those of safety and lack of toxicity after oral intake [1].

p-Aminobenzoic acid (PABA) has been known to be a nutritive supplement and a competative inhibitor of sulfonamides and diaminopyrimidines for the enzymes in folic acid synthesis [2]. On the contrary, antimicrobial activity of PABA itself has never been noticed until it was recently shown that this compound possessed inhibitory effect on some kinds of bacteria (unpublished data). This finding attracted further investigation because PABA is a very safely used substance. In man, it can be taken up until 12 g/day. If this compound is proved to have significant antimicrobial activity and is efficient to be applied as a preservative, it would be benefit in pharmaceutical fieled because there will be one more safe preservative to be in choice. In the present study, antimicrobial activity of PABA in various aspects were evaluated. Also, the application of this agent as a preservative in oral aqueous preparations, i.e., morphine mixture and frusemide suspension, was carried out.

Materials and Methods

Microorganisms

The bacterial strains studied were *Staphylococcus aureus* NCTC 10788, *Pseudomonas aeruginosa* NCTC 6750 and *Escherichia coli* NCTC 8110. The yeast strain applied was *Candida albicans* NCPF 3179.

Effect of solvent systems

PABA at 10% was prepared with 4 different solvent systems, i.e., absolute alcohol, alcohol:tween 20: water=5:1.5:3.5, propylene glycol and propylene glocol:glylcerine = 5:5 to give out 4 different stock solutions and at 2% was prepared with water (PABA could not be prepared as 10% solution because the compound was not dissolved completely). These solutions were then diluted in buffer. For each successive concentration, double strength of the compound was prepared and added into the broth. The antimicrobial sensitivity test of PABA was then performed.

Effect of pH

Nutrient broth (NB, Oxoid) or sabouraud dextrose broth (SDB, Oxoid) was prepared in double strength in phosphate buffer pH 6,7 and 8, and in alkaline borate buffer pH 8, 8.6 and 9. Double strength of PABA at various concentration was added and antimicrobial sensitivity test was then performed.

Oxidation-reduction reaction test

Phosphate buffer pH 5.0 and 7.4, was used. For each buffer pH, it was divided into three sets. The first set, 0.5 and 0.8 ml of 10% PABA (100 ml : PABA, 10 g; alcohol, 50 ml; tween 20, 15 ml; water, 35 ml) was added to 9.5 ml of phosphate buffer, pH 5.0 and 9.2 ml of phosphate buffer, pH 7.4, respectively. The second set, 0.1 ml of 10% sodium metabisulfite was firstly added and followed with 0.5 and 0.8 ml of 10% PABA to 9.4 ml of phosphate buffer, pH 5.0 and 9.1 ml of phosphate buffer, pH 7.4, respectively. The third set served as the control in which 0.1 ml of 10% sodium metabisulfite and 0.5 or 0.8 ml of cosolvents mentioned above were incorporated to buffer, pH 5.0 or 7.4 to obtain the final volume of 10 ml. In such incorporation, the final concentration of sodium metabisulfite became 0.1% whereas of PABA in buffer pH 5.0 and 7.4 were 0.5 and 0.8%, respectively. Tubes from each set were then treated in different conditions as follows : (i) heated at 100° C, 20 min; (ii) exposed directly to sunlight, 8 hours

and (iii) kept in a dark place, room temperature, 7 days. The results of oxidation-reduction reaction of PABA were deemed to occur if there was any color or other physical change observed.

Effect of an antioxidant

PABA at 10% was prepared as the stock solution with cosolvents which composed of alcohol, tween 20 and water as described earlier. The solution was then diluted in phosphate buffer, pH 6,7 and 8. For each successive concentration, 0.5 ml of double strength of the compound was prepared and added into 0.5 ml of double strength phosphate buffered broth, pH 6,7 and 8 which had been previously incorporated with 0.01 ml of 10% sodium metabisulfite (final concentration, 0.1%), the only antioxidant applied in the present study. The antimicrobial sensitivity test was then performed.

Antimicrobial sensitivity test

The test was carried out by broth dilution method as follows : double strength of NB or SDB was diluted 2-fold with double strength of PABA to give desired final concentrations, ranged between 0.025 and 1.0%. A 24-hour culture of bacteria in NB (incubated at 37° C) or 48-hour of yeast in SDB (incubated at 25° C) was diluted with the aforementioned broth to provide the test mixture of about 10^6 cells/ml after inoculation. The tests were incubated at 37° C, 18 hours for bacteria and at 25° C, 48 hours for yeast, unless otherwise specified. The minimum inhibitory concentration (MIC) of PABA was then read. For control, double strength of broth was mixed with equal volume of solvent or cosolvent. In the experiment with sodium metabisulfite, 0.1% of this antioxidant was also added into the control broth.

Maintenance of antimicrobial activity

PABA prepared in alcohol, tween 20 and water at 10% was duluted to be 1.6% with phosphate buffer, pH 6, 7 or 8. The equal volume of the latter solution was mixed with double strength phosphate buffered broth pH 6, 7 or 8. Tested microorganisms with density specified in antimicrobial sensitivity test were each inoculated into such PABA containing broth. The cultured broth was kept in room temperature for 3 months. The turbidity was then examined.

Efficacy as a preservative in pharmaceuticals

Morphine hydrochloride mixture (5 mg/5ml in 50 ml) and frusemide suspension (20 mg/5 ml in 50 ml) were kindly offered by M. Cormock, Pharmacy Department, Aberdeen Royal Informary, Aberdeen. They were prepared in a volume of 45 ml. The products were divided into three sets. The first set was added with 2.5 ml of cosolvents. The second set was added with 2.5 ml of 10% PABA. The third set was added with 0.5 ml of 10% sodium metabisulfite and subsequently with 2.5 ml of 10% PABA. The composition of the cosolvents and the preparation of 10% PABA were as described earlier. The volume of the products was finally adjusted with water to be 50 ml. The final concentrations of PABA and sodium metabisulfite in the preparations were 0.5 and 0.1%, respectively. The physical appearance of the aforementioned products was then observed after keeping in room temperature overnight. In consideration of pH, morphine mixture and frusemide suspension was also divided into three sets. The first set was adjusted with 2.5 ml of cosolvents and 2.5 ml of water. The second set was added with 0.5 ml of 10% sodium metabisulfite, 2.5 ml of cosolvents and 2 ml of water. The third set was incorporated with 2.5 ml of 10% PABA, 0.5 ml of 10% sodium metabisulfite and 2 ml of water. Each set was measured by pH meter within the day of the preparation.

The test procedure for examining the efficacy of PABA as an antimicrobial preservative in morphine mixture and frusemide suspension was carried out according to the method described in British Pharmacopeia [3]. Briefly, 18-hour cultures of *P. aeruginosa* NCTC 6750 and *E. coli* NCTC 8110 on soya tryptone agar (Oxoid) (incubated at 35° C) and 48-hour culture of *C. albicans* NCPF 3179 on SDA (incubated at 25° C) were washed, harvested and diluted with 0.1% peptone water (100 ml:peptone, 0.1 g; NaCl, 0.89 g) to give the density of about 1×10^8 cells/ml.

Each diluted culture was added into PABA with sodium metabisulfite containing morphine mixture and frusemide suspension as well as into controls (0.1% peptone water) to give about 1 X 10^6 cells/ml. Tests were done in duplicate in aliquots of 20 ml per preparation. The samples were taken for viable count after incubating the inoculated products at 25° C for 0, 6, 24 and 48 hours, 7, 14 and 28 days, respectively.

Reaction of the ingredient in tested pharmaceuticals with PABA

The ingredients in the tested morphine mixture were morphine hydrochloride, vanillin and saccharin. As the powdered form, they were each added into the solution of 0.5% PABA and the solution which consisted of 0.5% PABA and 0.1% sodium metabisulfite. The mixtures were shaken and the physical change was examined.

Results

Effect of solvent system and pH

The results in Table1 show that the solvent system had the effect but not much upon the antimicrobial activity of PABA. The best activity was observed when it was dissolved in alcohol while the worst when it was dissolved in propylene glycol with glycerine. In consideration of safety in use, stability and easiness in preparation, PABA in cosolvents consisted of alcohol, tween 20 and water was found to be most suitable and this solvent system was then chosen for solubilization of PABA in further work unless otherwise stated.

In terms of pH, it can be seen from Tables 1 and 2 that the antimicrobial activity of PABA was reciprocally proportional to pH. The greater the pH the lower the activity. The same Tables also revealed that the effect of PABA on microorganisms was affected by different buffer system. Better activity was observed in borate than in phosphate buffer.

Table 1 MIC of PABA prepared in different solvent systems which determined in phosphate buffered broth at different pH

Solvent (s)	pH	MIC (%) of PABA against			
		S. aureus	*P. aeruginosa*	*E. coli*	*C. albicans*
Water	6	0.1	0.05	0.1	0.4
	7	0.4	0.2	0.4	0.6
	8	0.4	0.4	0.4	0.6
Alcohol	6	0.1	0.1	0.1	0.4
	7	0.2	0.2	0.2	0.4
	8	0.4	0.4	0.4	0.6
Alcohol+Tween20+water	6	0.1	0.1	0.1	0.4
	7	0.4	0.2	0.4	0.6
	8	0.4	0.4	0.4	0.6
Propylene glycol	6	0.1	0.1	0.1	0.6
	7	0.4	0.2	0.4	0.6
	8	0.4	0.4	0.4	0.6
Propylene glycol+glycerine	6	0.1	0.1	0.1	0.4
	7	0.4	0.4	0.4	0.6
	8	0.6	0.6	0.6	0.6

Table 2 MIC of PABA prepared as the stock solution in water which determined in alkaline borate buffered broth at different pH

Microorganisms	MIC (%) of PABA at pH		
	8	8.6	9
S. aureus	ND*	ND	ND
P. aeruginosa	0.1**	0.4**	0.4***
E. coli	0.1	0.4	0.4
C. albicans	ND	ND	ND

* Not determined as the organism showed no growth in control after incubation for > 72 h

** Determined at 48 h as the organism showed no growth in control before that time

*** Determined at 72 h as the organism showed no growth in control before that time

Effect of antioxidant

It was shown in Table 3 that phosphate buffer containing PABA changed from the colorless to be the slightly yellowish solution after heat treatment as well as after exposing to light. When sodium metabisulfite, the antioxidant was incorporated, only the heated one could be protected from color change. Table 4 reveals that sodium metabisulfite itself also had the antimicrobial potential because no growth of *S. aureus* and *P. aeruginosa*, and slow growth of *E. coli* was observed after incubation at the specified time.

Table 3 Oxidation-reduction reaction of PABA in absence and presence of sodium metabisulfite incorporated into phosphate buffer treated at different conditions

Compound (s)* added	pH	Condition**	Physical appearance of the solution	Redox*** reaction
PABA (0.5%)	5.0	(i)	Slightly yellow	+
		(ii)	Slightly yellow	+
		(iii)	Colorless	-
PABA (0.5%) + sodium metabisulfite (0.1%)		(i)	Colorless	-
		(ii)	Slightly yellow	+
		(iii)	Colorless	-
PABA (0.8%)	7.4	(i)	Slightly yellow	+
		(ii)	Deep yellow	+
		(iii)	Colorless	-
PABA (0.8%) + sodium metabisulfite (0.1%)		(i)	Colorless	-
		(ii)	Slightly yellow	+
		(iii)	Colorless	-

* Controls which consisted of sodium metabisulfite (0.1%) and cosolvents were colorless at all three conditions tested

** See detail in Materials and Methods

*** + = oxidation - reduction reaction occured, - = oxidation -reduction reaction did not occur

Table 4 MIC of PABA prepared as the stock solution in cosolvents (alcohol, tween 20 and water) which determined in phosphate buffered broth in presence of sodium metabisulfite (0.1%)

Microorganisms	MIC (%) of PABA at pH		
	6	7	8
S. aureus	ND*	0.2	0.4
P. aeruginosa	ND	0.2**	0.4**
E. coli	0.05***	0.2	0.4
C. albicans	0.2	0.4	0.6

* Not determined as the organism showed no growth in broth which consisted of 0.1% sodium metabisulfite and cosolvents after incubation for > 72 h

** Determined at 48 h as the organism showed no growth in broth which consisted of 0.1% sodium metabisulfite and cosolvents before that time

*** Determined at 72 h as the organism showed no growth in broth which consisted of 0.1% sodium metabisulfite and cosolvents before that time

Maintenance of antimicrobial activity

Results in Table 5 showed that no microbial growth appeared in the inoculated broth containing PABA at 0.8% which kept for 3 months at room temperature.

Efficacy as a preservative in pharmaceuticals

After adding of PABA into the tested morphine mixture, it was remarkably observed that the clear colorless mixture turned rapidly to be deep yellowish green color (Table 6). In the presence of sodium metabisulfite, this incidence still remained. For frusemide suspension, it turned from white to be light brown after adding PABA and kept overnight. However, the color was unchanged when PABA was added together with sodium metabisulfite although the products were stored for more than one month (data not shown). Because color change in morphine mixture adding with PABA was not protected by sodium metabisulfite, each ingredient of this mixture was then tested for the possibility of making such appearance. Table 7 shows that vanillin was able to react with PABA to give the color (yellowish green) which was the same color as that appeared in morphine mixture stated above. Because vanillin was just only an additive, therefore, the efficacy test of PABA as the preservative in this mixture was still carried on.

Table 5 Shelf-life (determined at Day 90) of PABA (0.8%) prepared as the stock solution in cosolvents (alcohol, tween 20 and water) which determined in phosphate buffered broth in consideration of antimicrobial activity

Microorganisms	pH 6	pH 7	pH 8
S. aureus	NG*	NG	NG
P. aeruginosa	NG	NG	NG
E. coli	NG	NG	NG
C. albicans	NG	NG	NG

* NG = no growth

Table 6 Physical appearance of morphine hydrochloride mixture and frusemide suspension after adding with 0.5% PABA with 0.1% sodium metabisulfite

Products	Component (s) added*	Physical appearance
Morphine mixture	Cosolvents	Colorless solution
	PABA	Yellowish green solution
	PABA and sodium metabisulfite	Yellowish green solution
Frusemide suspension	Cosolvents	White suspension
	PABA	Light brown suspension
	PABA and sodium metabisulfite	White suspension

* See detail in Materials and Methods

Table 7 Reaction between the ingredients in morphine hydrochloride mixture and PABA (0.5%) prepared as the stock solution in cosolvents (alcohol, tween 20 and water)

Ingredient	PABA* added	Sodium metabisulfite* added	Appearance of the solution
Morphine hydrochloride	+	+	Colorless
	+	-	Colorless
Vanillin	+	+	Yellowish green
	+	-	Yellowish green
Saccharin	+	+	Colorless
	+	-	Colorless

* + = added, - = not added

Table 8 pH of morphine hydrochloride mixture and frusemide suspension after adding 0.1% sodium metabisulfite and 0.5% PABA with 0.1% sodium metabisulfite

Products	Component (s) added*	pH
Morphine mixture	Cosolvents	4.9
	sodium metabisulfite	3.45
	PABA and sodium metabisulfite	3.65
Frusemide suspension	Cosolvents	5.0
	sodium metabisulfite	4.45
	PABA and sodium metabisulfite	4.1

* See detail in Materials and Methods

Table 9 Efficacy of PABA as a preservative in morphine mixture and frusemide suspension

Products	Component (s) added*	Challenged microorganisms	Viable cells (CFU/ml)** at time						
			o h	6 h	24 h	48 h	7 d	14 d	28 d
Morphine mixture	Cosolvents	*P. aeruginosa*	$2.0x10^6$	$8.3x10^3$	0	0	ND***	ND	ND
		E. coli	$1.8x10^6$	$1.3x10^6$	$3.3x10^4$	0	ND	ND	ND
		C. albincans	$1.1x10^6$	$2.2x10^6$	$1.5x10^6$	$1.3x10^6$	$1.3x10^6$	ND	ND
	Sodium metabisulfite (0.1%)	*P. aeruginosa*	$8.5x10^5$	0	0	0	0	0	0
		E. coli	$1.2x10^6$	0	0	0	0	0	0
		C. albicans	$2.8x10^6$	$8.0x10^5$	0	0	0	0	0
	PABA (0.5%)+sodium metabisulfite (0.1%)	*P. aeruginosa*	$9.1x10^5$	0	0	0	0	0	0
		E. coli	$9.2x10^5$	0	0	0	0	0	0
		C. albicans	$2.1x10^6$	6	0	0	0	0	0
Frusemide suspension	Cosolvents	*P. aeruginosa*	$2.2x10^6$	$8.6x10^5$	$8.3x10^4$	$5.6x10^2$	ND	ND	ND
		E. coli	$1.8x10^6$	$1.2x10^6$	$8.9x10^5$	$6.1x10^2$	ND	ND	ND
		C. albicans	$9.8x10^5$	$1.2x10^6$	$1.2x10^6$	$1.0x10^6$	ND	ND	ND
	Sodium metabisulfite (0.1%)	*P. aeruginosa*	$9.3x10^5$	$7.0x10^2$	0	0	0	0	0
		E. coli	$9.0x10^5$	$6.5x10^4$	1	0	0	0	0
		C. albicans	$5.0x10^6$	$1.7x10^6$	$8.0x10^3$	$1.2x10^4$	$7.0x10^6$	$3.0x10^8$	$9.1x10^8$
	PABA (0.5%)+sodium metabisulfite (0.1%)	*P. aeruginosa*	$9.1x10^5$	0	0	0	0	0	0
		E. coli	$1.0x10^6$	0	0	0	0	0	0
		C. albicans	$5.0x10^6$	1	0	0	0	0	0

* See detail in Materials and Methods

** CFU/ml = colony forming unit/ml

*** Not determined

Since sodium metabisulfite had powerful antioxidative property upon PABA, this compound was concomitantly added into the products for further experiments. Table 8 shows the pH of the products, it was found that the pH of morphine mixture and frusemide suspension dropped after incorporating with PABA and sodium metabisulfite as well as with sodium metabisulfite alone. The products with these two different additive component (s) showed no significant difference in pH.

When the challenge test was performed in morphine mixture and frusemide suspension containing PABA and sodium metabisulfite, the complete eradication of the tested bacteria and yeast occured within 6 hours (Table 9). In morphine mixture containing sodium metabisulfite alone, however, was unable to detect the viable cells of the tested bacteria and yeast within 6 and 24 hours, respectively, while in frusemide suspension, the tested bacterial strains were undetected within 24-48 hours whereas *C. albicans* showed persistence of growth up until the final day of the test (28 days). On the contrary, the tested bacteria could survive in morphine mixture mixed with cosolvents alone (no PABA or sodium metabisulfite) for more than 6 to 24 hours, and yeast showed growth for more than 48 hours (the final day of the study). In frusemide suspension without PABA or sodium metabisulfite, the challenged bacteria and yeast could survive for more than 48 hours.

Discussion

It has been known that alcohol can enhance the activity of many chemical antimicrobial agents. This appearance also demonstrated in the present study. As shown in Table 1, PABA in alcohol showed better antimicrobial effect than in other solvent systems. On the contrary, a number of surface active agents can produce a greater reduction in the effectiveness of antimicrobial agents. In presence of tween 20, however, the inhibitory effect of PABA was not inactivated or remarkably reduced.

There are several factors exist which can influence the activity and stability of an antimicrobial agent[4]. In a pharmaceutical formulation which needs a suitable preservative, the pH of a product should be considered first during the selection[5]. For certain weak carboxylic acids such as benzoic acid, sorbic acid, the degree of antimicrobial effect of these compounds being pH dependent[6] and they generally exhibit much greater activity in acidic than in neutral or alkaline preparations. The same appearance also observed in PABA. The fact that most pharmaceuticals are alkaline pH while most preservatives are active in acidic pH. It was therefore, in the present study to see whether PABA retained the antimicrobial activity up until pH 9. In this investigation, alkaline borate buffer was chosen and PABA showed the effect in this buffer, pH 9. The same study also revealed that at the same pH level, PABA demonstrated better activity in borate than in phosphate buffer. This incidence might be because the borate buffer itself which had some inhibitory effect was able to potentiate the activity of PABA.

Many common compounds used in pharmaceutical field can undergo oxidation and PABA is one among them. In this study, it showed quite clearly that this compound was oxidized remarkably after exposing to light and heat. Also, the deterioration of PABA which was due to heat could be protected by sodium metabisulfite. In consideration of antimicrobial activity, better effect of PABA in the presence of this antioxidant was observed. The potentiative antimicrobial activity of PABA by sodium metabisulfite might be explained in two ways (i) the latter protected against oxidative degradation of the former, thus full existing activity of PABA exhibited and (ii) the latter itself had some inhibitory effect, thus actively increased the antimicrobial spectra of the former.

When the shelf-life in terms of antimicrobial effect was determined, such property maintained in the preparations at least 3 months after keeping at room temperature.

An overall study presented here demonstrated that PABA possessed the property which would be suitable to be used as a preservative. In order to get more efficacy and safty usage, it is likely to apply this compound in preparations which are in acidic pH or which consisting of ingredients/excipients possessing some antimicrobial/antioxidative activity. Because there are various reports revealed that aqueous suspensions are mostly contaminated while syrups, emulsions and solutions are found on occasions to contain viable microorganisms [7,8], it is, therefore,

more strongly recommended of using the preservatives in the suspensions. In this study, the preservative property of PABA, however, was tested in both acidic solution and suspension.

When PABA was applied in morphine mixture, the colorless solution turned to be the greenish yellow product and this color change still remained although in the presence of sodium metabisulfite. Finally, it was found that such greenish yellow color was due to the reaction between PABA and vanillin. Also, PABA altered the color of frusemide suspension but this incidence was protected by sodium metabisulfite. For the color happened in morphine mixture after adding of PABA seemed to be beneficial because the preparation was naturally colorized by the reaction of the ingredients themselves without adding any coloring agent, and the antimicrobial activity of PABA was unaffected either. Table 9 demonstrates that PABA with sodium metabisulfite in morphine mixture could inactivate *P. aeruginosa*, *E. coli* and *C. albicans* effectively within 6 hours, and so could in frusemide suspension. Since morphine mixture adding with sodium metabisulfite alone also showed promising antimicrobial effect, in economic point of view, this type of preparation might not be worth to incorporate again with PABA unless quicker antimicrobial activity was needed. However, in sodium metabisulfite containing frusemide suspension, the tested bacterial cells were completely eradicated within 24-48 hours but *C. albicans* showed growth for more than 28 days. Therefore, this type of preparation has to be preserved and PABA is one compound which should be considered to be involved in the preservative system. However, the ability of PABA to inactivate the most commonly occuring contaminants, e.g., gram-positive spore formers, gram-negative rods especially *Pseudomonas* isolated from contaminated products, moulds, as well as the maintenance of preservative efficacy at the end of the claimed shelf-life of the products should be examined in order to give strong recommendation of using PABA as the preservative in any pharmaceuticals.

References

1. Allwood, M.C. and Shaw, R.J.S. (1987) Preservation of mixtures, suspensions and syrups, In Preservatives in Food, Pharmaceutical and Environmental Industries, The Society of Applied Bacteriology, Technical Series No. 22, Blackwell Scientific Publications, New York, p. 197-210.
2. Franklin, T.J. and Snow, G.A. (1981) Biochemistry of antimicrobial action, 3rd ed., Chapman & Hall, Lodon.
3. British Pharmacopoeia Commision. (1988) Efficacy of antimicrobial preservatives, In British Pharmacopeia, vol 2, HMSO, London, p. A200-A203.
4. Lachman, L. (1968). The instability of antimicrobial preservatives. *Bull. Parenteral Drug Assoc.* 22, 127-144.
5. Rosen, W.E. and Berke, P.A. (1973) Modern concepts of cosmetic preservation. *J. Socie. Cosmetic Chem.* 24, 663-675.
6. Ecklund, T. (1983) The antimicrobial effect of dissociated and undissociated sorbic acid at different pH levels. *J. Appl. Bact.* 54, 383-389.
7. Baird, R.M., Crowden, C.A., O'Farrell, S.M. and Shooter, R.A. (1979) Microbial contamination of pharmaceutical products in home, *J. Hygiene*. 83, 277-283.
8. Baird, R.M. and Petrie, P.S. (1981) A study of microbiological contamination of oral medicaments. *Pharm. J.* 226, 10-11.

ฤทธิ์การต้านจุลชีพของพารา-อะมิโนเบนโซอิคแอซิดและการประยุกต์ใช้เป็นสารกันเสียในเภสัชผลิตภัณฑ์

มาลิน จุลศิริ ภ.บ., ปร.ด. *
*ไมเคิล อี ริชาร์ด ภ.บ., ปร.ด., วท.ด.***

บทคัดย่อ

พารา-อะมิโนเบนโซอิคแอซิด (พาบา) แสดงฤทธิ์ยับยั้งเชื้อ *สแตไฟโลคอคคัส ออเรียส* เอ็นซีทีซี 10788, *ซูโดโมนัส แอรูจิโนซา* เอ็นซีทีซี 6750, *เอสเชอริเชีย โคลี* เอ็นซีทีซี 8110 และ *แคนดิดา แอล-บิแคนส์* เอ็นซีพีเอฟ 3179 ระบบตัวทำละลายที่แตกต่างกันและสภาพความเป็นกรดที่ต่างกันส่งผลกระทบต่อฤทธิ์ของการต้านเชื้อของสารนี้ ฤทธิ์การต้านเชื้อดีขึ้นเมื่อละลายพาบาในแอลกอฮอลและสภาพความเป็นกรดที่ต่ำลงช่วยเพิ่มผลการยับยั้งของมัน ในทำนองเดียวกัน ฤทธิ์ของสารดังกล่าวเพิ่มขึ้นเมื่อมีโซเดียมเมตาไบซัล-ไฟท์อยู่ด้วย ภายหลังการตั้งสารละลายของพาบาไว้ในอุณหภูมิห้องเป็นเวลา ๓ เดือน ฤทธิ์การยับยั้งเชื้อทดสอบยังคงเดิม เมื่อเติมสารละลายนี้ในความเข้มข้น 0.5% ลงในสารละลายมอร์ฟีน และสารแขวนตะกอนฟลูซิไมด์ ปรากฏว่าสามารถยับยั้งเชื้อทดสอบข้างต้นได้ภายใน 6 ชั่วโมง (ไทยเภสัชสาร ปีที่ 15(4) : หน้า 243-253 (2533))

* ภาควิชาจุลชีววิทยา คณะเภสัชศาสตร์ มหาวิทยาลัยมหิดล กรุงเทพฯ 10400 ประเทศไทย
** โรงเรียนเภสัชศาสตร์ สถาบันเทคโนโลยีโรเบิร์ตกอดอน อะเบอดีน เอบี 9 1 เอฟอาร์ ประเทศสก๊อตแลนด์