Advance Publication by J-STAGE
Published online 24 June 2017
KONA Powder and Particle Journal /Doi:10.14356/kona.2018008 Original Research Paper

Photostability of Risperidone in Tablets †

Yuki Fujisawa [1]*, Yoshiteru Takahashi [1], Reiko Teraoka [2] and Shuji Kitagawa [2]

[1] *Pharmaceutical Technology Center, Sawai Pharmaceutical Co., Ltd., Japan*
[2] *Laboratory of Pharmaceutical Technology, Kobe Pharmaceutical University, Japan*

Abstract

The purpose of this study is to evaluate the photostabilization mechanism of risperidone tablets. Risperidone is widely used for sensory integration disorder. It is formulated as tablets, orally disintegrating tablets, fine granules, oral solutions, and intramuscular injections. We found that risperidone was unstable in tablets and generated oxidized products. Formation of the oxidized product R5 was promoted in the presence of hydroxypropylcellulose by photoirradiation. On the other hand, photostability improved greatly when carmellose (CMC) or carmellose calcium (CMC-Ca) was used as a disintegrant. Since CMC and CMC-Ca are acidic substances, the photostability of tablets may have been affected by pH. Therefore, the effects of different pHs were examined. Risperidone was dissolved in methanol and the buffer (in the presence or absence of hydroxypropylcellulose) at different pHs (1.2, 3.0, 4.0, 5.0, and 6.8) was added. The photodegradation of risperidone was not observed at less than pH 3.0 in the presence of hydroxypropylcellulose, and low pHs improved the photostability of risperidone. On the other hand, risperidone solution without hydroxypropylcellulose was stable at all pH values. Therefore, risperidone was photochemically oxidized in the presence of hydroxypropylcellulose at high pHs.

Keywords: photostability, risperidone, carmellose, pH, hydroxypropylcellulose, tablet

1. Introduction

Risperidone (3-{2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl}-6,7,8,9-tetrahydro-2-methyl-4H-pyrido [1,2-α] pyrimidin-4-one) is a benzisoxazol derivative that is widely used for sensory integration disorder (Janssen P.A.J., 1987); it has both serotonin 5-HT_2 and dopamine D_2 antagonistic activities (Janssen P.A.J. et al., 1988; Leysen J.E. et al., 1988; Grant S. and Fitton A., 1994).

Risperidone was developed by Janssen Pharmaceutica Inc. and won FDA approval in the US on December 29, 1993 (where it is marketed as RISPERDAL™), and subsequently achieved worldwide acceptance (Germann D. et al., 2012).

9-Hydroxylation of risperidone is mainly generated by two cytochrome P-450 enzymes, CYP2D6 and CYP3A4. 9-Hydroxyrisperidone is the major metabolite of risperidone in plasma. 9-Hydroxyrisperidone has pharmacological activity as well as risperidone (Yasui-Furukori N. et al., 2001).

Risperidone is formulated as tablets, orally disintegrating (OD) tablets, fine granules, oral solutions (Berus P. et al., 2005), and intramuscular injections. It is practically insoluble in water, freely soluble in methylene chloride, and sparingly soluble in ethanol. It dissolves in dilute acid solutions (Merck Index, 14th ed., 2006).

This active pharmaceutical ingredient (API) is hydrolyzed into the R2 form in the presence of water, and is also oxidized into the R5 form during preservation (Tomar R.S. et al., 2004; Bharathi Ch. et al., 2008). R5 is an N-oxide product of risperidone and one of the major degraded substances that is generated by photoirradiation. The chemical structures of risperidone, R2, and R5 are shown in **Fig. 1**.

OD tablets are a new type of solid dosage form that are easily dispersed or dissolved in the oral cavity and are swallowed without water. The compliance and acceptability of patients are improved by OD tablets (Rahman Z. et al., 2010). The EP (European pharmacopoeia) describes OD tablets as uncoated tablets intended to be placed in the mouth where they disperse rapidly before being swallowed and as tablets which should disintegrate within 3 min. FDA defines OD tablet as a solid dosage form which contains a medicinal substance or active ingredient which disintegrates rapidly within a matter of seconds when placed upon a tongue (Bhatu P.B. et al., 2011).

In the case of tablets that are unstable to light, film coating technology may be performed to improve the sta-

† Received 30 July 2015; Accepted 26 April 2017
J-STAGE Advance published online 24 June 2017
[1] 3-8, Akagawa 1-chome, Asahi-ku, Osaka 535-0005, Japan
[2] 19-1 Motoyamakita-machi 4-chome, Higashinada-ku, Kobe 658-8558, Japan
* Corresponding author: Yuki Fujisawa
E-mail: y.fujisawa@sawai.co.jp
TEL: +81-6-6926-2650 FAX: +81-6-6922-5952

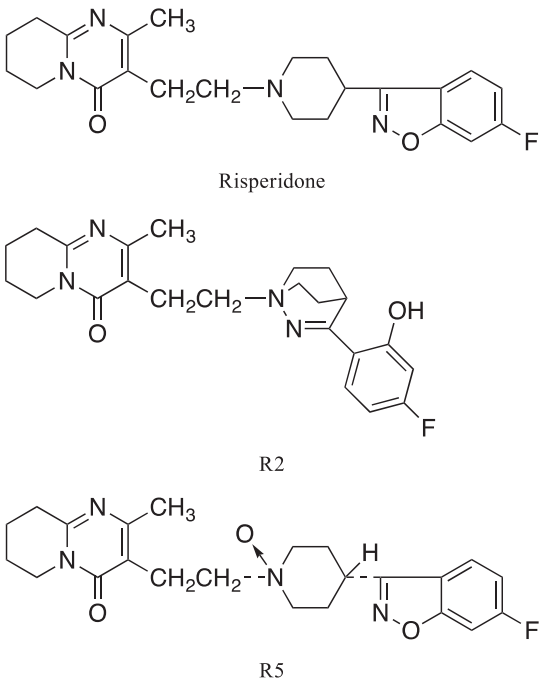

Fig. 1 Structural formulas of risperidone, R2, and R5.

bility. For example, titanium oxide, which is often formulated in the film has light shielding properties. However, film coating technology is not applicable to OD tablets because the film does not dissolve promptly with saliva. Also, the surface of the OD tablet is often brittle, the surface may collapse during film coating.

To develop the optimal formulation for risperidone OD tablets, the effects of excipients on the stability of risperidone were investigated.

When the risperidone OD tablets were previously formulated, the stability of risperidone against heat and photoirradiation was improved by adding carmellose (CMC) (Iwakura Y. et al., JP Patent, P2013-60392A).

It is well established that photochemical reactions of API are often affected by the excipients. Testing of the photostability of a drug substance and of the final dosage form is important to ensure the life span of the product (Tønnesen H.H., 2001).

The purpose of this study is to evaluate the stabilization mechanism of risperidone and other additives in risperidone OD tablets against photoirradiation.

2. Materials and methods

2.1 Formulation and manufacturing methods of risperidone orally disintegrating tablets

The formulation of risperidone OD tablets is shown in **Table 1**.

Risperidone was obtained from Assia Chemical Industries Ltd. (Israel) for JP grade. Aspartame was JPE grade. Other materials were JP grade.

Table 1 Formulation of risperidone OD tablets.

	Ingredient	Weight (mg/tab)
1	Risperidone	0.5
2	D-Mannitol	q.s.
3	Corn Starch	3.0
4	Anhydrous Dibasic Calcium Phosphate	10.0
5	Carmellose (CMC)	5.0
6	Carmellose Calcium (CMC-Ca)	5.0
7	Hydroxypropylcellulose (HPC)	0.5
8	Light Anhydrous Silicic Acid	0.75
9	Magnesium Stearate	0.5
10	Aspartame	2.0
11	Flavor	0.15
	Total	50.0

HPC was obtained for L grade of NISSO HPC (Nippon-Soda, Japan).

The OD tables were prepared by three different manufacturing methods as follows.

Method A: From No. 1 to No. 6 in **Table 1** were mixed in a fluidized bed granulator and then granulated by 1 % (w/w) HPC aqueous solution. The granules were sieved using a 710 μm screen and excipients from No. 8 to No. 11 were mixed. The mixture was compressed using a tablet press.

Method B: From No. 1 to No. 7 in **Table 1** were mixed in a fluidized bed granulator and then granulated using purified water. The granules were sieved using a 710 μm screen and excipients from No. 8 to No. 11 were mixed. The mixture was compressed using a tablet press.

Method C: From No. 1 to No. 6 in **Table 1** were mixed in a fluidized bed granulator and then granulated by purified water. Additionally, 1 % (w/w) HPC aqueous solution was sprayed for granulation. The granule was sieved using a 710 μm screen and excipients from No. 8 to No. 11 were mixed. The mixture was compressed using a tablet press.

Fluidized bed granulator: Multiplex Coater (MP-01, Powrex, Japan). Tablet press: PICCOLA (RIVA S.A., Argentina).

2.2 Irradiation test of risperidone OD tablets

Sample tablets of methods A, B, and C were stored in a light-irradiation tester with a D65 lamp (LT-120, Nagano Science, Japan), as previously demonstrated (Teraoka R.

et al., 2001).

Irradiation was carried at 1000 lx for 25 days. The temperature in the light-irradiation tester was kept at 298 K.

2.3 High-performance liquid chromatography (HPLC)

The analysis of risperidone and its degradation forms by an HPLC system in tablets has been reported (Suthar A.P. et al., 2009). The R5 formation rate was analyzed with an HPLC system (Prominence UFLC, Shimadzu, Japan) equipped with a UV detector (SPD-20AV, Shimadzu, Japan) operated at 275 nm. The packaged column was a reverse-phase C18 column (Zorbax SB-C18, 3.5 µm, 3.0×150 mm, Agilent, USA) operated at 298 K. The flow rate was kept at 1.1 mL/min. The mobile phase consisted of purified water:acetonitrile:trifluoroacetic acid (1600: 400:3) and the pH value was adjusted to 3.0 by adding NH_3 solution. After photoirradiation, 5 risperidone OD tablets were added into 25 mL of 0.1 mol/L hydrochloric acid/methanol mixture (3:2). After shaking, this solution was filtered using a polyolefin disposable syringe filter (Chromatdisk 25A, 0.45 µm, GL Science, Japan). A total of 10 µL of sample solution was subjected to HPLC analysis.

2.4 Colorimetric measurement

The color of a sample tablet was measured with a chromameter (Spectrophotometer SE6000, Nippon Denshoku, Japan) with the L*a*b* colorimetric system.

The average of 5 tablet measurements of ΔE^*, before and after photoirradiation in the 3-dimensional $L^*a^*b^*$ color space, was calculated as follows.

$\Delta E^* = [(\Delta L^*)^2 + (\Delta a^*)^2 + (\Delta b^*)^2]^{1/2}$

ΔL^*: the lightness difference

Δa^*: the red/green difference

Δb^*: the yellow/blue difference

2.5 Preparation of sample powders

The sample powders of risperidone and other additives were prepared as described in **Table 2**.

2.6 Solid-state UV-VIS spectra

UV-VIS solid-state absorption spectra of samples from a) to d) were measured on a UV-2450 system (Shimadzu, Japan) equipped with an integrating sphere unit (Shimadzu ISR-2200) at room temperature. A cell was filled with sample powder and the spectra were acquired with 0.2 nm sampling pitch in the wavelength range from 300 to 400 nm.

Table 2 Preparation of sample powders.

	Sample	Preparation Method
a)	RIS/CMC (powder)	7.5 g of risperidone and 7.5 g of CMC were mixed using a pestle in a mortar for 2 min.
b)	RIS/CMC (pellet)	7.5 g of risperidone and 7.5 g of CMC were mixed and granulated in a mortar with 3 mL of purified water. The granules were dried at 343 K for 2 h by a hot air circulation-type constant-temperature oven (MO-921, Toyama Sangyo, Japan).
c)	RIS/HPC (powder)	7.5 g of risperidone and 7.5 g of HPC were mixed using a pestle in a mortar for 2 min.
d)	RIS/HPC (pellet)	7.5 g of risperidone and 7.5 g of HPC were mixed and granulated in a mortar with 3 mL of purified water. The granules were dried at 343 K for 2 h by a hot air circulation-type constant-temperature oven (MO-921, Toyama Sangyo, Japan).

Table 3 Formulation of different amounts of CMC in risperidone OD tablets.

	Ingredient	Weight (mg/tab)		
	(Amount of CMC)	0	2.5	5.0
1	Risperidone	0.5	0.5	0.5
2	D-Mannitol	q.s.	q.s.	q.s.
3	Corn Starch	3.0	3.0	3.0
4	Anhydrous Dibasic Calcium Phosphate	10.0	10.0	10.0
5	CMC	0	2.5	5.0
6	CMC-Ca	5.0	5.0	5.0
7	HPC	0.5	0.5	0.5
8	Light Anhydrous Silicic Acid	0.75	0.75	0.75
9	Magnesium Stearate	0.5	0.5	0.5
10	Aspartame	2.0	2.0	2.0
11	Flavor	0.15	0.15	0.15
	Total	50.0	50.0	50.0

2.7 Solid-state NMR

^{13}C CP/MAS NMR spectra of samples a)~d) were measured on a Varian NMR System 500 with a zirconia sample tube (outer diameter: 5 mm, scanning speed: 20 kHz).

2.8 Formulation of sample tablets to examine the effect of CMC amount on stability

To examine the effect of CMC in tablets on photostability, three different amounts of CMC in tablets were prepared, as shown in **Table 3**. All formulations were manufactured by method C described in 2.1. Sample tab-

lets were stored at 1000 lx for 14 days and R5 was measured by HPLC.

2.9 Formulation of sample solutions to examine the effect of pH on stability

A total of 1 mL of 0.5 mg/mL risperidone in methanol was mixed with 2 mL of 1 % (w/w) HPC buffer solution with various pHs (1.2, 3.0, 4.0, 5.0, 6.8). Sample solution was injected in a quartz cell and stored in a light-irradiation tester with a D65 lamp (3500 lx) for 14 days. The R5 formation rate was analyzed by HPLC. Each pH of buffer solution is shown as follows.

pH 1.2: 1st fluid for dissolution test (JP)
pH 3.0: Dilute McIlvaine buffer solution, pH 3.0
pH 4.0: Dilute McIlvaine buffer solution, pH 4.0
pH 5.0: Dilute McIlvaine buffer solution, pH 5.0
pH 6.8: 2nd fluid for dissolution test (JP)

2.10 Formulation of sample solutions to examine the effect of HPC concentration

A total of 1 mL of 0.5 mg/mL risperidone in methanol was mixed with 2 mL of each concentration (0 %, 0.01 %, 0.1 %, 1 %) of HPC buffer solution at pH 6.8. Sample solution was injected in a quartz cell and stored in a light-irradiation tester with a D65 lamp (3500 lx) for 14 days. The R5 generation rate was analyzed by HPLC.

3. Results and discussion

3.1 Photostability of risperidone OD tablets by different manufacturing methods

Tablets produced by methods A, B, and C were subjected to accelerated stability testing at 1000 lx for 25 days using a D65 lamp. The R5 formation rate was measured by HPLC and color differences were measured using a chromameter.

The results of photostability testing are shown in **Table 4**. Comparing these three manufacturing methods in terms of stability, method A was most unstable and method C was most stable. Similarly, the most color change was observed in method A. The color difference in method C was very limited.

It was considered that method C is the most stable manufacturing method among these three methods.

Table 4 R5 formation rate and color difference of risperidone OD tablets after photoirradiation

Method	R5 formation (%)	Color difference (ΔE^*)
A	2.7	1.74
B	1.1	0.76
C	0.5	0.40

3.2 Measurement of solid-state UV-VIS spectra and solid-state NMR

There was a possibility that the change of photostability was due to a shift of the absorption wavelength (Kojima T. et al., 2007). Spectrum from 300 nm to 400 nm in a solid state was measured and the relative absorbance spectrum was plotted with the absorbance of 300 nm set as 1.0.

Sample d) was not measured because rubber-like pellets were obtained and these pellets were not suitable for the measurement because they were not solidified by the press.

As shown in **Fig. 2**, a shift of spectrum was not observed in any sample. Therefore, there was no change in the absorption wavelength.

Solid-state NMR has developed as an important technique for the characterization of pharmaceutical solids as well as DSC, FT-IR, and PXRD. Physicochemical information about both API and the formulated product was provided by the measurement (Berendt R.T. et al., 2006). It has been reported that risperidone has three polymorphs (Karabas I. et al., 2007; Krochmal B. et al., 2004). There was a possibility that the crystal form of risperidone was changed and a difference in the stability was observed. Measurements of samples a)~d) and risperidone were performed using solid-state NMR to determine whether the crystal form had changed or not and their spectra were compared. As shown in **Fig. 3**, changes in the spectra were not observed and it was suggested that there were no changes in the crystal forms.

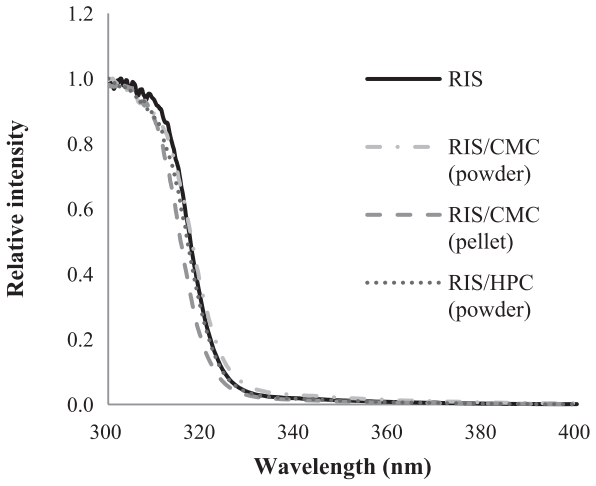

Fig. 2 Solid-state UV-VIS spectra of risperidone and samples a)~c).

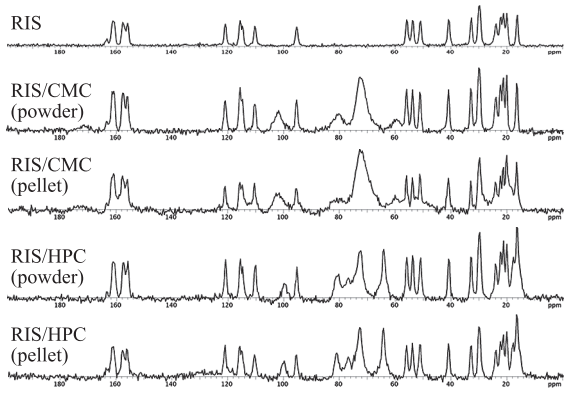

Fig. 3 Solid-state NMR spectra of risperidone and samples a)~d).

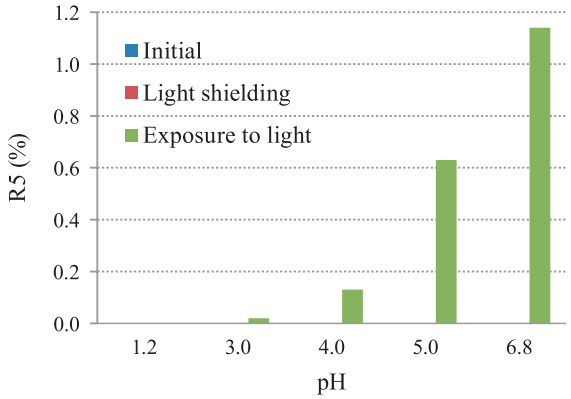

Fig. 4 R5 formation rate in different pH solutions (HPC concentration: 1 %).

3.3 Effect of CMC in tablets on the photostability

CMC is widely used as a relatively acidic disintegrant. A total of 1.0 g of CMC was dispersed in 100 mL of purified water and the suspension showed about pH 3.5 to 5.0 (European Pharmacopoeia 8th Edition, 2014).

To examine the effect of CMC on the photostability, three different amounts of CMC (0, 2.5, 5 mg) in OD tablets were formulated and stored at 1000 lx for 25 days. The pH of the tablet was also measured by dispersing the tablet in 20 mL of purified water for 20 min.

As the amount of CMC in the tablet increased, the pH value was lowered.

As shown in **Table 5**, No R5 was detected in any sample before photoirradiation by HPLC analysis. After photoirradiation, R5 was detected and its amount varied in a CMC-dependent manner.

3.4 R5 formation rate in different pH solutions

The R5 formation rate of risperidone/HPC solution at different pHs was investigated. The results of photostability testing are shown in **Table 6** and **Fig. 4**. In light shielding conditions, all samples were stable. When samples were exposed to light, R5 was generated at high-pH conditions. It is considered that the photostability of risperidone was affected by the pH of the solution.

3.5 R5 formation rate at different hydroxylpropylcellulose concentrations

To evaluate the effect of HPC on the stability of API, risperidone was dissolved in different concentrations of HPC aqueous solution. As shown in **Table 7**, R5 formation was not observed at any sample in light shielding conditions. On the other hand, R5 formation was increased with increasing HPC concentration when samples were exposed to light.

Table 5 R5 formation rate at different amounts of CMC in OD tablets

CMC (mg/tab)	pH	R5 formation rate (%)	
		Initial	1000 lx 25 days
0	7.6	N.D.	4.14
2.5	6.0	N.D.	1.31
5.0	5.1	N.D.	0.87

Table 6 R5 formation rate at different pH solutions (HPC concentration: 1 %).

pH	R5 formation rate (%)		
	Initial	3500 lx 14 days	
		Light shielding	Exposure to light
1.2	N.D.	N.D.	N.D.
3.0	N.D.	N.D.	0.02
4.0	N.D.	N.D.	0.13
5.0	N.D.	N.D.	0.63
6.8	N.D.	N.D.	1.14

Table 7 R5 formation rate at different HPC concentrations (pH 6.8)

HPC (%)	R5 formation rate (%)		
	Initial	3500 lx 14 days	
		Light shielding	Exposure to light
0	N.D.	N.D.	N.D.
0.01	N.D.	N.D.	0.07
0.1	N.D.	N.D.	0.15
1	N.D.	N.D.	0.86

4. Conclusions

By the difference of manufacturing method, the photostability of risperidone in OD tablets was changed.

The photostability was significantly improved by adding purified water before granulation. These differences in stability suggested that risperidone and HPC reacted upon photoirradiation and formed degradation substances.

From the analysis of solid-state UV-VIS spectrum and solid-state NMR, no physical change was observed.

At low pH, risperidone in HPC solution was stable upon photoirradiation. On the other hand, risperidone in HPC solution was stable at any pH under light shielding conditions. It is suggested that this photo-reaction is suppressed at low pH because risperidone has mono- and di-protonated forms (pK_1 = 8.1–8.6, pK_2 = 3.1) (Alparone A., 2011).

The photostability of risperidone in HPC solution depended on the concentration of HPC.

To improve the photostability of risperidone OD tablets, it is important to use acidic excipients and a small amount of HPC.

Nomenclature

API	active pharmaceutical ingredient
CMC	carmellose (carboxymethylcellulose)
CMC-Ca	carmellose calcium
DSC	differential scanning calorimetry
EP	European pharmacopoeia
FDA	Food and drug administration
FT-IR	Fourier transform infrared spectroscopy
h	hour
HPC	hydroxypropylcellulose
JP	Japanese pharmacopoeia
lx	lux
min	minute
N.D.	not detected
NMR	nuclear magnetic resonance
OD	orally disintegrating
PXRD	powder X-ray diffraction
q.s.	quantum sufficiat
tab	tablet
w	weight

References

Alparone A., Spectroscopic properties of neuroleptics: IR and Raman spectra of Risperidone (Risperdal) and of its mono- and di-protonated forms, Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 81 (2011) 631–639.

Berendt R.T., Sperger D.M., Isbester P.K., Munson E.J., Solid-state NMR spectroscopy in pharmaceutical research and analysis, TrAC Trends in Analytical Chemistry, 25 (2006) 977–984.

Berus P., Gartner A., Mlakar A., Puncuh K.A., Vrecer F., Preparation of a stable oral solution with risperidone, European Journal of Pharmaceutical Sciences, 25S1 (2005) S57–S58.

Bharathi Ch., Chary D.K., Kumar M.S., Shankar R., Handa V.K., Dandala R., Naidu A., Identification, isolation and characterization of potential degradation product in risperidone tablets, Journal of Pharmaceutical and Biomedical Analysis, 46 (2008) 165–169.

Bhatu P.B., Atish S.M, The technologies used for developing orally disintegrating tablets: A review, Acta Pharmaceutica, 61 (2011) 117–139.

European Pharmacopoeia 8th Edition, Carmellose, Carmellose calcium, The European Directorate for the Quality of Medicines & HealthCare, 2014, pp. 1773–1774.

Germann D., Kurylo N., Han F., Risperidone, Chapter 8 in: Brittain H. (Eds.), Risperidone, Profiles of drug substances, excipients, and related methodology, Academic Press, 37, 2012, pp. 313–361.

Grant S., Fitton A., Risperidone: A Review of its pharmacology and therapeutic potential in the treatment of schizophrenia, drugs, 48 (1994) 253–273.

Iwakura Y., Fujisawa Y., Toyonaga N., Oral disintegrant tablet containing risperidone and method for producing the same, JP Patent, (2013) JP2013060392A.

Janssen P.A.J., The development of new antipsychotic drugs: Towards a new strategy in the management of chronic psychoses, Journal for Drugtherapy and Research, 12 (1987) 324–328

Janssen P.A.J., Niemegeers C.J.E., Awouters F., Schellekens K.H.L., Megens A.A.H.P. and Meert T.F., Pharmacology of risperidone (R 64 766), a new antipsychotic with serotonin-S_2 and dopamine-D_2 antagonistic properties, Journal of pharmacology and experimental therapeutics, 244-2 (1988) 685–693.

Karabas I., Orkoula M.G., Kontoyannis C.G., Analysis and stability of polymorphs in tablets: The case of Risperidone, Talanta, 71 (2007) 1382–1386.

Kojima T., Onoue S., Katoh F., Teraoka R., Matsuda Y., Kitagawa S., Tsuhako M., Effect of spectroscopic properties of tamoxifen citrate polymorphs, International Journal of Pharmaceutics, 336 (2007) 346–351.

Krochmal B., Diller D., Dolitzky B., Aronhime J., Preparation of risperidone, US Patent (2004) US6,750,341B2.

Leysen J.E., Gommeren W., Eens A., de Chaffoy de Courcelles D., Stoof J.C., Janssen P.A., Biochemical profile of risperidone, a new antipsychotic, The Journal of Pharmacology and Experimental Therapeutics, 247 (1988) 661–670.

Merck Index, 14th ed., Merck Research Laboratories, division of Merck & Co., Whitehouse Station, N.J., , 2006, entry 8316, 1478.

Rahman Z., Zidan A.S., Khan M.A., Risperidone solid dispersion for orally disintegrating tablet: Its formulation design and non-destructive methods of evaluation, International Journal of Pharmaceutics, 400 (2010) 49–58.

Suthar A.P., Dubey S.A., Patel S.R., Shah A.M., Determination

of Risperidone and forced degradation behaviour by HPLC in tablet dosage form, International Journal of PharmTech Research, 1 (2009) 568–574.
Teraoka R., Konishi Y., Matsuda Y., Photochemical and oxidative degradation of the solid-state tretinoin tocoferil, Chemical & pharmaceutical bulletin, 49 (2001) 368–372.
Tomar R.S., Joseph T.J., Murthy A.S.R., Yadav D.V., Subbaiah G., Krishna Reddy K.V.S.R., Identification and characterization of major degradation products of risperidone in bulk drug and pharmaceutical dosage forms, Journal of Pharmaceutical and Biomedical Analysis, 36 (2004) 231–235.
Tønnesen H.H., Formulation and stability testing of photolabile drugs, International Journal of Pharmaceutics, 225 (2001) 1–14.
Yasui-Furukori N., Hidestrand M., Spina E., Facciolá G., Scordo M.G., Tybring G., Different enantioselective 9-hydroxylation of risperidone by the two human CYP2D6 and CYP3A4 enzymes, Drug Metabolism and Disposition, 29 (2001) 1263–1268.

Author's short biography

Yuki Fujisawa

Yuki Fujisawa graduated from Nagoya City University in 2002 and the Graduate School of the same university in 2004. He received a degree in organic and medicinal chemistry from the Graduate School. He has worked for Sawai Pharmaceutical Co., Ltd., since 2007. He is responsible for formulation development and scale-up study as a pharmaceutical researcher.

Yoshiteru Takahashi

Yoshiteru Takahashi is an executive corporate officer of Sawai Pharmaceutical Co., Ltd. He received BS degree (1975), Master degree (1977) and Ph.D. (1985) in pharmaceutical science from Kyoto University. He joined Sawai Pharmaceutical Co., Ltd. in 2003. His research interests include formulation development, scaling-up and improvement of the manufacturing technologies in a manner that allows for production on the market and enables registration.

Reiko Teraoka

Reiko Teraoka, Ph.D. is currently associate professor of laboratory of pharmaceutical technology in Kobe Pharmaceutical University.

Her research interests focus on:

• Stability evaluation and stabilization design of pharmaceutical drugs

Photostability of solid pharmaceutical drugs and cocrystals in particular

• Proper use of transdermal fentanyl for palliative care and anti-AIDS agent

Shuji Kitagawa

Shuji Kitagawa is a Professor in Department of Pharmaceutical Technology at Kobe Pharmaceutical University. Since April, 2013 he has also been a President of the same university. He holds a Ph.D. degree from Kyoto University in 1981. His research interests include percutaneous permeation of polyphenols and rheological study on ointments and creams. He has published more than 100 research papers during his research career.