MANAS Journal of Engineering
ISSN 1694-7398 | e-ISSN 1694-7398

Volume 9, Issue 2, (2021) Pages 129-135
https://doi.org/10.51354/mjen.918635

Toxicity of polyvinyl alcohols in medicinal chemistry

Orkun Dalyan[*1], Ömer Faruk Öztürk[2], Mehmet Pişkin[*3]

[1]Çanakkale Onsekiz Mart University, School of Graduate Studies, Department of Occupational Health and Safety, Çanakkale, Turkey, orkundalyan@outlook.com, ORCID: 0000-0003-4791-9084

[2]Çanakkale Onsekiz Mart University, Faculty of Arts and Sciences, Department of Chemical, Çanakkale, Turkey, ofozturk@comu.edu.tr, ORCID: 0000-0002-9244-6805

[3]Çanakkale Onsekiz Mart University, Vocational School of Technical Sciences, Department of Food Processing, Çanakkale, Turkey, mehmetpiskin@comu.edu.tr, ORCID: 0000-0002-4572-4905

ABSTRACT

Polyvinyl alcohol (Chemical Abstracts Service No: 9002-89-5), biodegradable, biocompatible, water-soluble, odorless, tasteless, transparent, white to creamy granular or powder appearance, and is a synthetic hydroxy polymer used in a broad variety of industrial, trading, medicinal and food implementations. The aim of this review is to back the safety of polyvinyl alcohol qua a coating agent for medicinal chemistry and dietary addition products, considering the current knowledge of polyvinyl alcohol. All available information on polyvinyl alcohol obtained from a comprehensive scientific literature review was seriously evaluated. Orally directed polyvinyl alcohol is comparatively harmless. The safety of polyvinyl alcohol when directed orally is based on: (a) Acute oral toxicity LD50 rates are in the range of 14.7–20 g/kg, very low, (b) is very poorly absorbed from the digestive system, (c) does not accumulate in the body, (d) the highest levels of polyvinyl alcohol with no observed adverse effects when directed orally in male and female rats, 5000 mg / kg body weight / day in a 90-day diet survey as the highest dose tested and 5000 mg / kg body weight / day was found in two generation reproductive studies.

ARTICLE INFO

Review article

Received: 17.04.2021
Accepted: 17.05.2021

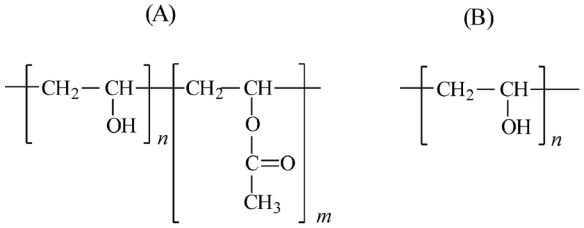
Keywords:
polyvinyl alcohol,
toxicity,
medicinal chemistry,
dietary supplement,
coating material

**Corresponding author*

1 Introduction

Polyvinyl alcohol (PVOH) is an odorless, tasteless, transparent, biodegradable, biocompatible, water-soluble hydroxy synthetic polymer with a white to creamy granule or powder appearance [1]. With its high tensile strength, heat and chemical resistance, water solubility and flexibility properties, PVOH has been used in a broad variety of industrial, trading, medicinal and food implementations, including resins, varnishes, surgical threads and food contact implementations since the early 1930s. It is obtained by partial and complete hydrolysis of polyvinyl acetate. It is not toxic or carcinogenic. It shows stability in different temperature and pH ranges. Its resolution occurs at 80 ºC. It has the formula (C2H4O)x. Its density is 1.19-1.31 g / cm³ and its melting temperature is 230 ° C. [2,3].

The physical properties of PVOH depend on the process of preparedness from the hydrolysis or local hydrolysis of polyvinyl acetate (Figure 1). PVOH is usually divided into two groups, locally hydrolyzed (A) and completely hydrolyzed (B).



Changing the extent of the first vinyl acetate polymer and the grade of hydrolysis under alkaline or acidic conditions constitutes PVOH products of different molecular weights (20,000-400,000), solvability, elasticity, tensile force and stickiness. To characterize PVOH, various properties are determined like pH, viscosity, drying deprivation, melting point, refractive index, heavy metals and ruins in combustion. These characteristics change depending on the molecular weight and% hydrolysis for the degree of PVOH.

PVOH is involved in the Pharmaceutical Excipients Handbook. Identifications for pharmaceutical usage are supplied in Japanese Pharmaceutical Excipients, United States of America Pharmacopoeia / National Formulary and European Pharmacopoeia. Pharmaceutical grade PVOH must be produced under CGMP standards. Pharmaceutical grades further need lower impurities and residual solvent grades than industrial grades.

In the US, most of PVOH is used as a sizing and finishing agent in the textile industry. PVOH can further be included into a water-solvable cloth in the output of degradable preventive clothing, laundry bags for hospitals, diapers, sponges, sheets, coatings, and further physiological hygiene products.

PVOH is further broadly used in the output of paper products. Like with textiles, PVOH is applied as a sizing and coating agent. It ensures rigidity to these materials and becomes useful in tube wrapping, cardboard sealing and cardboard lamination. PVOH is used in paint and common household white glue. It is also used as a thickening agent in gypsum-based cements such as those used for ceramic tiles. PVOH is comparatively insolvable in organic solvents and its solvability in aqueous solutions can be adapted to its required implementation [4].

The US Food and Drug Administration (US FDA) allows PVOH to be used as an indirect food contribution in food contact products (Table 1).

Table 1. *PVOH approved food contact uses (US FDA)*

Section	Title
175.300	Resin and polymeric coatings
175.320	Resinous and polymeric coatings for polyolefin films
175.380	4-4′- Xylene-formaldehyde resins thickened with isopropylidene diphenol epichlorohydrin epoxy resins
175.390	Zinc-silicon dioxide matrix coatings
176.170	Paper and cardboard components that come into contact with aqueous and fatty foods
176.180	Paper and cardboard components in contact with dry food
177.1200	Selofan
177.1210	Sealed lids for food containers
177.1400	Hydroxyethyl cellulose film insoluble in water
177.2260	Resin-bonded filters
177.2800	Textile and textile fibers
178.3910	Surface lubricants used in the manufacture of metallic products
181.30	Substances used in the manufacture of paper and cardboard products used in food packaging

According to Federal Regulation 21 CFR 73.1 (b) (2), PVOH is confirmed as a diluent in color contribution mixtures to color shell eggs and further under Federal Regulation 21 CFR 349.12, PVOH is confirmed as an ophthalmic sedative of 0.1-4.0%.

PVOH is approved for use in the packaging of meat products by the Meat Inspection Division of the United States Department of Agriculture, and for use in the packaging of poultry products by the United States Department of Agriculture's Poultry Division. PVOH has been approved for use in a variety of medicinal implementations, involving the preparation of gels that dry quickly when applied to the skin, as well as prompt and sustained release tablet formulations. Cross-linked PVOH microspheres are further used for the controlled release of oral drugs. Ophthalmic solutions, like synthetic tears, may include PVOH as they ensure good dispersion and coating properties (2). PVOH is involved in the FDA Inactive Ingredients Guidelines for ophthalmic preparations and oral tablets. As an industrial and trading product, PVOH is rated for its solvability and biodegradability, which conduces to its truly low environmental effect. Various microorganisms ubiquitous in synthetic and natural environments like septic systems, garbage dumps, compost and soil that can degrade PVOH through enzymatic processes have been identified [4]. A compound of oxidase and hydrolase enzyme activities reduces PVOH to acetic acid, but not only the percentage of hydrolysis but its solvability impact the biodegradation grade of PVOH. There are further potential food uses for PVOH that are now being evaluated, involving uses in candy products and high humidity food products. The aim of this review is to back this crucial assessment of current knowledge on PVOH and the safety of PVOH as a coating agent for pharmaceutical and dietary supplement products.

2. Biological Data

Absorption, distribution and excretion of PVOH (mol. Weight <50,0001) was worked in male and female Fischer 344 rats [5]. Over 98% of a sole oral dose of 0.01mg / kg 14C-labeled PVOH directed to three male rats was saved in the feces within 48 hours of implementation. Less than 0.2% of the total dose was detected in urine. No radioactivity from PVOH was detected as expired 14CO2 or volatiles. There was no detectable tissue collecting. These data show that very little PVOH is absorbed from the gastrointestinal tract. To further evaluate the possible bio collecting, 0.1 mg / kg body weight / day of 14C-labeled PVOH was directed to three additional mice by gavage for 10 consecutive days. Similar consequences were found in the first study, almost all radioactivity saved 0.2% of the total dose in feces, urine and 0.05% of the total dose detected in major tissues (blood liver, kidneys, skin, muscle, and adiposis) [5].

3. Toxicity Studies

3.1. Acute toxicity

The consequences of the acute toxicity works are summarized in Table 2. These data suggest that orally directed PVOH would fall in the "comparatively harmless" category of the fewest concern [6].

Table 2. *PVA between acute oral LD 50*

Species	LD50 (mg / kg)	Reference
Rat	> 20.000 *	Zaitsev et al., 1986 [7]
Rat	21.500	Clydesdale, 1997 [8]
Mouse	147.000	Zaitsev et al., 1986 [7]
Mouse	> 4000 *	Burford and Chappel, 1968 [9]
Dog	20.000	Clydesdale, 1997 [8]

* The highest dose administered.

3.2. Dermal toxicity

Short-Term: Pure PVOH (1.0 ml / kg for 1000 mg / kg dose) was implemented to the shaved skin of 20 albino rats (10 of each breed) 5 days a week for 5 weeks and every day once a day (27 in total). Daily observations were made. Blood samples were taken after 16 hours of fasting. Animals were autopsied. No differences in body weights, and visual view were seen between cured and control animals. Mean hematocrit and red blood cell worth were notably under for cured men comparison to controls ($p < .05$). No change was found to be associated with PVOH treatment at autopsy [10].

Sub-Chronic: Ten female albino rats were cured 5 times per week for 13 weeks with a peelable face mask involving 13% PVOH. The test material was implemented to the shaved back skin. Because of the growing skin irritation and worries about the survival of the animals, a face mask was applied. It was erased after a 15-minute exposure in the 3rd week. Subsequently, the test standard was followed again. Skin irritation is balanced. After blood samples were taken at 6 and 13 weeks, hematological and serum chemistry parameters were measured. An autopsy was done. No important toxic impacts were found to be associated with the test material [11].

3.3. Parenteral toxicity

Short-Term: In a study by Hueper [12], 12 albino rats (70-88 g) obtained 20 injections (1 ml) of 5% PVOH solution over a period of 4 weeks. One of the 6 rats died during dosing, the remaining five mice were killed for autopsy after 2 weeks. The pathological changes of the animals killed 2 weeks after dosing were more violent. There was a significant quantity of PVOH at the injection site, consequence in necrosis and granulomatous purulent tissue. Very few of the applied PVOH was determined in lymph nodes. PVOH aggregates were concentrated in the glomeruli of the kidneys. PVOH was found to remain dispersed in the lumen of blood vessels of various organs and occlude the lumen by forming globules. Vascular occlusion was particularly seen in the lungs of some rats. Enlarged endothelial cells with foamy cytoplasm were seen in the occluded capillaries. Histiocytes in a variety of tissues involved PVOH in granular form. Of the parenchymal cells, those containing PVOH were the ganglion cells of the brain, renal tubular epithelium, and adrenal cortical cells. The spleens were darker red in color, moderate enlarged and hard. A grow in the number and swelling of Kupffer cells was observed in the liver of all rats. Other organs were quite normal but had little foam cell groups. Hueper (12) further applied 5% PVOH solution to three male rabbits at 10-15-25 doses for 5 days. Resulting were likewise those observed in rats, with the exclusion that the most violent and broad lesions were detected in the lungs, spleen, and testes following intravenous implementation, whereas the hypodermic route resulted in marked replaces in the kidneys, liver, and spleen.

Hall and Hall [13] conducted a hypertension work with female Houston-Cheek rats weighing 65-75g. He gave 1 ml of 5% PVOH solution in physiological saline daily for 28 days four groups of seven animals. While the test material was directed hypodermically to groups 1 and 2, it was directed intraperitoneally to groups 3 and 4. The PVOH used in the study had a mean molecular weight of 133,000. After the 28th day of dosing, treatment groups 2 and 4 were given an injection of 0.1 mg d-aldosterone-21 acetate twice daily in sesame oil for 7 successive days. Other groups were given vehicle injections only. Non-PVOH dosed control groups (5 and 6) received hormones in vehicle or were left uncured. Sufficient feed and water were ensured; systolic blood pressures were obtained regularly and besides before and after aldosterone implementation. Four animals died during the 28-day interval after the PVOH dose and before aldosterone or vehicle cure. The mean blood pressure of each group was: (1) 208, (2) 204, (3) 252, (4) 225, (5) 137, and (6) 141 mm Hg. Three animals further died after the week of aldosterone cure; One of these three animals in group 4 developed acute peripheral edema and ascites. Other animals were killed, organs were weighed, and tissues were analyzed microscopically. All rats in surviving groups 1 and 3 treated with PVOH and vehicle injections alone developed hypertension. Although the oppression increased from 208 to 213 mm Hg in group 1 animals, it stayed the same in group 3 animals. Except for PVOH implementation, a decrease in blood pressure was observed in rats treated with hormone only. Blood pressure in the animals in group 2 reduced from 204 to 187 mm Hg and in the animals in group 4 from 225 to 208 mm Hg. Blood pressures were comparatively unmodified between 141 and 136 mm Hg in group 5 and 137 to 128 mm Hg in group 6. In checks, aldosterone cure lonely did not induce or compound hypertension. At autopsy, the heart, liver, spleen, and kidneys of the PVOH-treated rats were importantly heavier than the other organs. Further, the heart

and kidneys were importantly heavier in rats treated intraperitoneally compared to those treated hypodermic. Adrenal glands were littler in animals treated with aldosterone. After all, the adrenal glands were importantly lesser in the PVOH groups than in the untreated controls. Remarkable histopathological changes involved dilated hepatic sinusoids in rats cured with PVOH, plentiful multinucleated huge cells in the livers of those cured intraperitoneally, large numbers of PVOH accrued in the spleen and kidneys and involved intense macrophage and huge cell proliferation. Hypertrophy, inflammatory changes and necrosis were present in the splenic arteries in rats with hypertension. Polyarteritis nodosa was detected in the pancreas of 5 of 13 rats given subcutaneous PVOH. In the hearts of rats treated intraperitoneally, foam cell transformation of the arterial site or foam cells was detected. Peritubular sclerosis and blown and ischemic glomeruli and thickened capillaries were observed in the kidneys of a few rats. He stated that no lesions could be particularly ascribed to aldosterone cure.

Riviere et al. [14] used pureblood Beagle dogs to define whether PVOH-induced toxicosis could give qua a model for glomerulonephritis. A silastic cannula was surgically implanted in the right outer jugular vein of four dogs. Three dog were dedicated daily injections owing to the cannula of 20 ml solutions including 47 mg PVOH/ml; the fourth dog was injected with saline. The PVOH used had a molecular weight of 125,000 and was 88% hydrolyzed. Blood samples were contained routine for the definition of blood urea nitrogen (BUN) and packed cell volume (PCV) rates. Urine samples were taken fortnightly. At the end of intervention, blood and urine samples were acquired for full analysis and autopsy was done. After 1 week of intervention, a reduce in PCV was watched. At the end of the study, the rates fell by 64% of the original rate. No changes in BUN were detected. A rise in the certain gravity of urine was detected; nevertheless, the rise lonely could not define the proteinuria which consisted by the end of the study. Body weight, feed consumption, and gastrointestinal task stayed normal. The study was finished after 3 weeks of dosing owing to low grade central nervous system (CNS) depression as specified by mutual depression of the extensor postural thrust, hopping, front limb placing, and rear limb righting reflexes. After the work cured animals had reduced total serum protein, sodium, potassium, and phosphorus concentrations. Hematologic analysis observed monocities, immature neutrophilia, marked polymorphonuclear leukocyte toxicity, reduced PCV, reduced hemoglobin, and reduced erythrocyte counts, slight anisocytosis, and many huge platelets. No gross lesions were detected. Light microscopic inspection observed diffuse vacuolation of the red pulp cells in the spleen and formation of foam cells in the glomeruli. No changes in the brain were detected. In electron micrographs, a granular sediment was present on the luminal surface of most endothelial cells. Mesangial cells and, to a less degree, endothelial and epithelial cells had cytoplasmic vacuolation. Because anemia and CNS depression happened before development of important renal injury, the analysts refused the usefulness of PVOH induced glomerulonephritis in the dog as a model for working glomerular disorders.

Hall and Hall [13] done a work using female Holtzman rats and three solutions of PVOH of diverse molecular weight to define the effect of the grade of polymerization. Groups of 12 rats taken daily hypodermic injections of 1 ml of 5% PVOH dissolved in physiological saline. The degrees of PVOH used had molecular weights of 37,000 (low), 133,000 (medium), or 185,000 (high). The fourth group became the control group and taken just vehicle. The animals were given feed and distilled water to drink as much as. It was measured hebdomadal blood pressures and everyday liquid intake of animals. Systolic pressures larger than 150 mm Hg were think hypertensive. So that it was investigated tissues and organs, these animals were killed after 29 days. PVOH was not determined in any of organs and tissues. Nonetheless it was determined that one third of the animals of cure group rise of blood pressure. The high molecular weight PVOH collected in a number of organs and tissues and reasoned puffing and multiplication of endothelial and epithelial cells of the renal glomeruli. One of the two the animals in the loud molecular weight cured group improved slight hypertension and some organs grown. The intermediate polymer was the just 1 out of 3 tested that made polydipsia. In the consequence nephrotic syndrome, ascites and oedema were come with by strong hypertension, evidenced renal harm with violent glomerulonephritis, and widespread cardiovascular lesions. Animals of this cured group finished on the mean more of the salt dispersion than them of the alternative groups. The analysts think about that molecular dimension rather than chemical structure effected the toxic effects and lesion development.

Carver et al. [15] recorded everyday hypodermic (1 ml) doses of 5% watery PVOH of mid molecular weight (133,000) directed for 21 days to male Sprague-Dawley rats resulted in a benign glomerulopathy with collecting of the macromolecule in the glomerular mesangium. These rats afterwards had an early temporal dose related sensibility to gentamicin nephrotoxicity. After all, after 12 days of daily dosing with gentamicin, no variation was discovered in the response of PVOH-cured rats as compared to non-cured controls.

Sub-Chronic: Burgener, Gutierrez, and Logsdon [16] used injections of PVOH spalls in male crossbred dogs to develop a model of hepatic cirrhosis. Portal hypertension and hepatic fibrosis were induced using PVOH in size from between 100-400 microns then the spalls were suspended using in 0.9% NaCl dispersion. To protect portal hypertension in 20 cm of water, injections of 0.1 to 0.9 g of PVOH once a week or two weeks were required. Sole doses to be given daily and per dog

were detected by portal vein pressure. The total dose requirements differentiated between dogs. It was from 0.8 g implementation over 22 months in the Four fraction to 4.8 g implementation over 6 months in the 14 fractions.

3.4. Short-term vaginal toxicity

A PVOH sponge was put into the vagina of each of three New Zealand white adult female rabbits weighing 4-5 kg and kept for 10 days [17]. After the animals were killed and the vaginas of each were investigated with light and electron microscopy. No differences were detected with light microscopy in the vaginal tissue as compared to samples from other controls. Microvilli electron microscopy and cell boundaries showed minimal irritation. A 30-day intravaginal PVOH study in B6C3F1 mice was done by the National Toxicology Program (NTP) [18]. Two groups of 50 female mice were cured with 25% PVOH implementations for 30 days (intravaginally daily). Animals of one group were kept for a few minutes following each implementation and only one control animal was treated with vehicle. As well as no deaths during dosing, no effects on body weight or total weight rise were found. Only some animals had vaginal irritation and expansion of the uterine horns.

3.5. Dermal irritation

Patches involving 0.3 ml of 10% PVOH in distilled water of unspecified molecular weight were implemented to groups of four female albino rabbits (Kb1: JW). The substance was implementation to the cut off back for 24-hours of contact. One group's skin was eroded. Skin affects were scored with respect to the Draize scoring system at the time of darn removal and 72 hours after removal. The Primary Irritation Index (PII) was 0.2 (maximum score 8.0). Erythema was noted at the 24-hour seen in three of four rabbits with eroded skin. No reaction was detected during the 72-hour observation [19]. No dermal irritation was observed in nine rabbits sustained once to undiluted PVOH in an occlusive darn. Watching were made at 2 and 24 hours after opening of wrapping. In another study on 6 rabbits following the alike method, irritation was minimum. In the 2-hour observation, it was stated that five animals had 1 point (maximum score 8). The reactions of three of the five animals continued at 1 point at 24-hour observation [20].

3.6. Dermal sensitization

A group of five Hartley albino pigs was used in a modified maximization test of 10% PVOH in fractionated water [21]. On the first day of induction, Freund's Complete Adjuvant (FCA) emulsified in distilled water, 10% PVOH in distilled water and 10% PVOH emulsified with FCA were injected intradermally into the nape. One week later, 10% sodium lauryl sulfate (SLS) in petrolatum was implemented to the region. One day following SLS cure, 0.2 ml of PVOH was implemented under a 48-hour occlusive darn. The control group of four animals was cured with distilled water following the same process. After 3 weeks following the first induction; 0.1 ml PVOH was implemented under an occlusive darn to the flank. Reactions were monitored 24 and 48 hours after implementation, but no reaction was seen.

3.7. Ocular irritation / toxicity

Knight and Link [22] researched diverse substances to find a proper coating for intraocular lenses (IOLS) made of polymethylmethacrylate (PMMA) in order to decrease corneal endothelial cell deprivation. To measure research, freshly cut rabbit corneas were contacted to the coating substance and then exposed to endothelial cell staining. On a scale of 0-4, with 0 being no damage and 4 being extensive damage (>50%); the uncured PMMA lens scored mean of 2.5 after static touch and mean of 3.6 after dynamic touch, and the PVOH cured cornea pointed mean of 0.7 after static touch and mean of 0.8 after dynamic touch. These analysts further notified three in vivo toxicity analysis for PVOH. In the first analysis, five times the quantity of PVOH as would a lens was injected into the front chamber of one sphere in each of 12 rabbits. Saline solution was injected into the other sphere as a control. Intraocular pressure (IOP), slot-lamp inspections and entire-eye microscopic works were applied routinely for 6 months. No important difference was observed between control and experimental eyes. In the second analysis, radioactive PVOH was injected into the front chamber of the eyes of 21 rabbits. In the tissue samples received, almost half of the directed dose was excreted in the urine within 48 hours by the kidneys after clearing the sphere within 45 minutes. PVOH was not determined in any organ, involving the sphere. In the third analysis, 20 IOLs (10 coated, 10 uncoated) were injected one-sidedly in 20 cats. A sham operation was applied on the toward eye. Endothelial cell calculates, IOP quantity's, pachymetry and slot lamp examinations were made for 6 weeks postoperatively. A decrease in endothelial cell deprivation was detected in gloves implanted with a coated lens. No other differences were observed between check and cured spheres [22]. Even an only drop of undiluted PVOH into the conjunctival bag of six rabbits did not reason irritation. After operation, eyes were not washed and marked using the Draize standard (maximum score 110). Similar conclusions were stated in another study [23] that a peel-off mask including 13.0% PVOH did not reason ocular irritation in six rabbits.

3.8. Reproduction toxicity

PVOH was implemented in the diet to male and female Sprague Dawley rats (26 / sex / group) at doses of 0, 2000, 3500 and 5000 mg / kg body weight / day for two generations. The work design rated the gonadal function, estrus cycle, mating behavior, conception, pregnancy, birth, breastfeeding, weaning and growth and development of F1 and F2 offspring. Parent rats were cured 70 days before mating, until sacrificed for the periods of mating, pregnancy and lactation. Clinical

observations, body weights and feed consumption were registered always. Dietary concentrations were arranged for each gender to reach the intended levels of mg / kg / day of PVOH on a weekly basis, except during pregnancy and lactation. Puppies were continuously weighed and weaned at 21 days before selection for the next generation. Shapeless faeces were recorded predominantly at levels of 3500 and 5000 mg / kg body weight / day in P0 and F1 parent animals. This finding was ascribed to high levels of PVOH that was fed and then excreted in the faeces. Slight reduces in mean body weights of P0 men were registered in 2000 and 5000 mg / kg / day. Feed consumptions rise primarily at cured levels of 3500 and 5000 mg / kg / day in both generations but did not rise in either lactation period. These rises were usually detected in a dose-dependent manner (g / kg / day) as a consequence of consuming large quantities of PVA to maintain the calorie intake required for normal growth. PVOH had no effect on P0 or F1 male or female reproductive performance or offspring survival, growth, organ weights, and macroscopic or microscopic watching. Dietary concentrations of PVOH 2000, 3500, and 5000 mg / kg / day for male and female rats did not reason any adverse toxicological or reproductive effects in parent animals (P0 and F1) or F1 and F2 offspring. The NOAEL for this work was 5000 mg / kg, the highest dose tested [24].

4. Results and discussion

All usable knowledge on polyvinyl alcohol from a comprehensive scientific literature review was critically evaluated. Oral polyvinyl alcohol is comparatively innocuous. The safety of polyvinyl alcohol is based on:

(a) The acute oral toxicity of polyvinyl alcohol is very low and the mean lethal dose rates are in the range of 15-20 g / kg;
(b) orally implemented polyvinyl alcohol is very weakly absorbed from the digestive system;
(c) when implemented orally polyvinyl alcohol does not accumulate in the body;
(d) polyvinyl alcohol is not mutagenic or clastogenic; and
(e) The highest levels of polyvinyl alcohol directed orally in male and female rats were 5000 mg / kg body weight / day and 5000 mg / kg body weight / day in two generations of reproductive work, the highest dose tested in the 90-day dietary work. Orally directed polyvinyl alcohol is safe and appropriate for it choose to use qua a coating for dietary addition and pharmaceutical product tablets and capsules. Polyvinyl alcohol can be used in high moisture foods to maintain the overall satisfactory taste, texture and quality of the foods. Confectionery products may further include polyvinyl alcohol to maintain the integrity of moisture sensitive ingredients. It is used as a moisture barrier film for food addition tablets and for dry food containing inclusions that must be maintained from moisture absorption, or food containing inclusions.

Acknowledgments

This study was supported by the Office of Scientific Research Projects Coordination at Çanakkale Onsekiz Mart University. Project number: FHD-2021-3364.

References

[1]. Köysüren NH., Köysüren Ö., "Preparation of Polyvinyl Alcohol Composite Nanofibers and Solid-Phase Photocatalytic Degradation Polyvinyl Alcohol", Journal of The Faculty of Engineering and Architecture of Gazi University, 33, (2018), 1411-1418.

[2]. Wade A., Handbook of Pharmaceutical Excipients, Weller PJ, Ed. American Pharmaceutical Association, Washington DC. 1994.

[3]. Rowe RC., Sheskey PJ., Handbook of Pharmaceutical Excipients. Owen SC, Ed. Pharmaceutical Press and American Pharmacists Association, Washington DC. 2006.

[4]. Isolyser Company, 1998. Isolyser Company, Inc. 4320 International Boulevard, NW, Norcross, GA.

[5]. Sanders JM., Matthews HB., "Vaginal Absorption of Polyvinyl Alcohol in Fischer 334 rats", Human and Experimental al Toxicology, 9. (1990), 71 – 77.

[6]. Hodge HC., Sterner JH., "Tabulation of Toxicity Classes", American Industrial Hygiene Association Quarterly, 10, (1949), 93-96.

[7]. Zaitsev NA., Skachkova IN., Sechenov IM., "Substantiation of Hygienic Standards for some Polymeric Compounds in Water with the Use of Gradual Standardization", Gig Sanit, 10, (1986), 75-76.

[8]. Clydesdale FM., Food Additives: Toxicology, Regulation and Properties. CRC Press, Boca Raton, FL. 1997.

[9]. Burford, RG, Chappel C, 1968. Range-Finding Acute Toxicity Studies of Polyvinyl Alcohol, Phthalic Acid and Cellulose Acetate Phthalate in the Mouse. Bio-Research Laboratories, Ltd., Point Claire, Quebec. For: Merck, Sharpe and Dohme Research Laboratories, West Point, Penn./Charles E. Frosst & Company, Montrél, Unpublished study.

[10]. CTFA. 1975. Six-week subacute dermal toxicity study in rats: Polyvinyl Alcohol. Unpublished data submitted by the CTFA, June 20, 1995. (8 pages).

[11]. CTFA. 1977. Safety evaluation of peel-off mask: containing 13% Polyvinyl Alcohol. Thirteen-week subchronic dermal toxicity study in rats. Unpublished data submitted by the CTFA, June 20, 1995. (9 pages).

[12]. Hueper WC., "Organic Lesions Produced by Polyvinyl Alcohol in Rats and Rabbits", Archives of Pathology, 28, (1939), 510–531.

[13]. Hall CH., Hall O., "Polyvinyl Alcohol Nephrosis: Relationship of Degree of Polymerization to Pathophysiologic Effects", Proceedings of the Society for Experimental Biology Medicine, 112, (1963), 86-91.

[14]. Riviere JE., Coppoc GL., Carlton WW., Hinsman EJ., "Polyvinyl Alcohol Toxicosis as a model of Glomerulonephritis in Beagle Dogs", American Journal of Veterinary Research, 41, (1980), 502 – 505.

[15]. Carver MP., Monteiro-Riviere NA., Brown TT., Riviere JE., "Dose-Response Studies of Gentamicin Nephrotoxicity in Rats with Experimental Renal Dysfunction. II. Polyvinyl Alcohol Glomerulopathy", Toxicology and Applied Pharmacology, 80, (1985), 264 – 273.

[16]. Burgener FA., Gutierrez OH., Logsdon GA., "Angiographic, hemodynamic, and histologic evaluation of portal hypertension and periportal fibrosis induced in the dog by intraportal polyvinyl alcohol injections", Radiology, 143, (1982), 379 – 385.

[17]. Chvapil M., Chvapil TA., Owen JA., Kantor M., Ulreich JB., Eskelson C., "Reaction of vaginal tissue of rabbits to inserted sponges made of various materials", Journal of Biomedical Materials Research, 13, (1979), 1–13.

[18]. National Toxicology Program (NTP). 1992. 30-Day intravaginal study of PVOH in B 16C3F mice. Study No. 688066. Research Triangle Park, NC: NTP.

[19]. Shiseido Research Center. 1978. Primary skin irritation: Polyvinyl Alcohol. Unpublished data submitted by the CTFA, July 17, 1995. (3 pages).

[20]. Cosmetic, Toiletry, and Fragrance Association (CTFA). 1974. Primary skin irritation: Polyvinyl Alcohol. Test # 06-183. Unpublished data submitted by the CTFA, June 20, 1995. (1 page).

[21]. Shiseido Research Center. 1977. Contact allergenicity: Polyvinyl Alcohol. Unpublished data submitted by the CTFA, July 17, 1995. (3 pages).

[22]. Knight PM., Link WJ., "Surface Modification of Intraocular Lenses to Reduce Corneal Endothelial Damage", American Intra-Ocular Implant Society Journal, 5, (1979), 123 – 130.

[23]. CTFA. 1980. Eye irritation: Polyvinyl Alcohol. Test # 47-093. Unpublished data submitted by the CTFA, June 20, 1995. (1 page).

[24]. Colorcon. 2001. Polyvinyl Alcohol (PVA): Study of the Effects of PVA on Fertility, Early Embryonic Development to Weaning, and the Growth and Development when Directed in the Diet to Rats.